```
=> file caplus; d que l1
FILE 'CAPLUS' ENTERED AT 16:14:34 ON 16 MAR 2004
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FILE COVERS 1907 - 16 Mar 2004 VOL 140 ISS 12
FILE LAST UPDATED: 15 Mar 2004 (20040315/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

L1 1 SEA FILE=CAPLUS ABB=ON PLU=ON RIZZIERI D?/AU AND BIGNER D?/AU AND ZALUTSKY M?/AU

```
=> => file medline; d que l25; d que l26
FILE 'MEDLINE' ENTERED AT 16:16:02 ON 16 MAR 2004
```

FILE LAST UPDATED: 13 MAR 2004 (20040313/UP). FILE COVERS 1951 TO DATE.

On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD for details. OLDMEDLINE now back to 1951.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L25 0 SEA FILE=MEDLINE ABB=ON PLU=ON RIZZIERI D?/AU AND BIGNER D?/AU AND ZALUTSKY M?/AU

L26 0 SEA FILE=MEDLINE ABB=ON PLU=ON RIZZIERI D?/AU AND ZALUTSKY M?/AU

```
=> file embase; d que l32; d que l33
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```

FILE COVERS 1974 TO 11 Mar 2004 (20040311/ED)

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L32 0 SEA FILE=EMBASE ABB=ON PLU=ON RIZZIERI D?/AU AND BIGNER D?/AU AND ZALUTSKY M?/AU

L33 0 SEA FILE=EMBASE ABB=ON PLU=ON RIZZIERI D?/AU AND ZALUTSKY M?/AU

=> file biosis; d que l53
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 10 March 2004 (20040310/ED)

FILE RELOADED: 19 October 2003.

L53 2 SEA FILE=BIOSIS ABB=ON PLU=ON RIZZIERI D?/AU AND BIGNER D?/AU AND ZALUTSKY M?/AU

=> file wpid; d que 162
FILE 'WPIDS' ENTERED AT 16:16:37 ON 16 MAR 2004
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FILE LAST UPDATED: 16 MAR 2004 <20040316/UP>
MOST RECENT DERWENT UPDATE: 200418 <200418/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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>>> ADDITIONAL POLYMER INDEXING CODES WILL BE IMPLEMENTED FROM DERWENT UPDATE 200403.
THE TIME RANGE CODE WILL ALSO CHANGE FROM 018 TO 2004.
SDIS USING THE TIME RANGE CODE WILL NEED TO BE UPDATED.
FOR FURTHER DETAILS: http://thomsonderwent.com/chem/polymers/ <<<

```
L62             1 SEA FILE=WPIDS ABB=ON  PLU=ON  RIZZIERI D?/AU AND BIGNER D?/AU
                  AND ZALUTSKY M?/AU


=> dup rem l1 l53 l62
FILE 'CAPLUS' ENTERED AT 16:17:00 ON 16 MAR 2004
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FILE 'WPIDS' ENTERED AT 16:17:00 ON 16 MAR 2004
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PROCESSING COMPLETED FOR L1
PROCESSING COMPLETED FOR L53
PROCESSING COMPLETED FOR L62
L72             3 DUP REM L1 L53 L62 (1 DUPLICATE REMOVED)
                  ANSWER '1' FROM FILE CAPLUS
                  ANSWERS '2-3' FROM FILE BIOSIS

=> d ibib ab l72 1-3

L72  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2004 ACS on STN  DUPLICATE 1
ACCESSION NUMBER:         2002:504652  CAPLUS
DOCUMENT NUMBER:          137:59618
TITLE:                    Anti-tenascin monoclonal antibody therapy for lymphoma
INVENTOR(S):              Rizzieri, David; Bigner, Darell D.
                          ; Zalutsky, Michael
PATENT ASSIGNEE(S):       Duke University, USA
SOURCE:                   PCT Int. Appl., 29 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND  DATE          APPLICATION NO.   DATE
     ----------------    ----  --------      ---------------   --------
     WO 2002051448       A1    20020704      WO 2001-US46104   20011024
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
             US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2002187100       A1    20021212      US 2001-8062      20011019
     EP 1351713          A1    20031015      EP 2001-996085    20011024
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRIORITY APPLN. INFO.:                    US 2000-257108P  P  20001221
                                          WO 2001-US46104  W  20011024

AB   A method of treating lymphoma in a subject comprises administering to a
     subject afflicted with lymphoma an antibody that binds to tenascin in a
     therapeutically effective amount  Preferably the antibody is monoclonal
```

antibody 81C6 or an antibody that binds to the epitope bound by monoclonal antibody 81C6. Preferably the antibody is labeled with or conjugated to a chemotherapeutic agent, particularly a radioisotope such as 131I.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L72 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:474119 BIOSIS
DOCUMENT NUMBER: PREV200200474119
TITLE: Radioimmunotherapy of refractory non-Hodgkin's lymphoma with 131I-labeled chimeric 81C6 anti-tenascin monoclonal antibody: Dosimetry study.
AUTHOR(S): Akabani, G. [Reprint author]; **Rizzieri, D.** [Reprint author]; Coleman, R. E. [Reprint author]; Metzler, S. D. [Reprint author]; **Zalutsky, M. R.** [Reprint author]; **Bigner, D. D.** [Reprint author]
CORPORATE SOURCE: Duke University Medical Center, Durham, NC, USA
SOURCE: Journal of Nuclear Medicine, (May, 2002) Vol. 43, No. 5 Supplement, pp. 313P. print.
Meeting Info.: 49th Annual Meeting of the Society of Nuclear Medicine. Los Angeles, CA, USA. June 15-19, 2002.
CODEN: JNMEAQ. ISSN: 0161-5505.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 11 Sep 2002
Last Updated on STN: 11 Sep 2002

L72 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:152427 BIOSIS
DOCUMENT NUMBER: PREV200200152427
TITLE: Radiolabeled anti-tenascin antibody for refractory non-Hodgkins lymphoma (NHL).
AUTHOR(S): **Rizzieri, David A.** [Reprint author]; Akabani, Gamal; Coleman, R. Edward; **Zalutsky, Michael R.**; Niedzwiecki, Donna [Reprint author]; Payne, Nancy [Reprint author]; Wikstrand, Carol; **Bigner, Darell D.**
CORPORATE SOURCE: Division of Oncology and Stem Cell Transplantation, Duke University Medical Center, Durham, NC, USA
SOURCE: Blood, (November 16, 2001) Vol. 98, No. 11 Part 2, pp. 247b. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 2. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Feb 2002
Last Updated on STN: 26 Feb 2002

AB Tenascin (TN), an extracellular matrix glycoprotein that is significantly over-expressed in multiple tumor types, including breast cancer, lung cancer, GI tumors, brain tumors, and lymphomas. Interestingly, TN over-expression in tumorous tissue increases with more aggressive grades of lymphoma. Further, within the same patient, over-expression is limited to the tumor site. These data suggest the stroma of the tumor may be an attractive target for therapy. We have created a humanized murine antibody to tenascin and radiolabeled it with I-131. Patients with relapsed or refractory NHL who are not candidates for high dose therapy,

have not been previously radiated to tissue tolerance, do not have >25% marrow involvement with disease, have normal blood counts and adequate liver/renal function were eligible. We have treated 2 patients to date. The first had refractory well differentiated lymphoma following 3 different chemotherapy and rituximab regimens without any significant response. The second patient had diffuse large cell lymphoma refractory to 3 standard regimens of chemotherapy. For dosimetry, 10 mg of antibody was labeled with 10 mCi of I-131 and infused as a bolus. Following a week of daily gamma camera imaging and pharmacokinetic analyses, pts were treated with a therapeutic dose of 40 mCi I-131 conjugated to 10 mg of anti-tenascin antibody. No cold blocking antibody was given prior to labeled dose in this phase I trial. The whole-body, visceral organ, and tumor dosimetry are given. The whole-body effective half life and residence time in patient 1 was 116 hours and 167 hours respectively and for patient 2 was 109 hours and 158 hours, respectively. Even without a cold dose for blocking of non-specific uptake, the tumor still concentrates the radiolabeled antibody at a ratio of 5X over visceral organs. Each patient noted 1 night sweat and mild diarrhea the night of therapy, and low grade fever persisting for a few days. Both patients experienced transient myelosuppression occurring between weeks 4-6 from therapy. With early follow up of 1-3 months, both have responded with decreased tumor size, though the maximum response is not yet determined. The above dosimetry estimates and prolonged residency time are very encouraging. The increased TN expression in more aggressive lymphomas and many other tumors such as breast cancer, lung cancer, and gastrointestinal malignancies suggests this targeted radiotherapy may have broad applicability. These results, as well as the clinical outcomes for the patients, support further evaluation of anti-stromal targeted therapy with radiolabeled, anti-tenascin antibody.

```
=> file hcaplus; d que l12; d que l14; d que l15; d que l18; d que l19
FILE 'HCAPLUS' ENTERED AT 16:19:06 ON 16 MAR 2004
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FILE COVERS 1907 - 16 Mar 2004  VOL 140 ISS 12
FILE LAST UPDATED: 15 Mar 2004  (20040315/ED)

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 substance identification.


L2         14585 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LYMPHOMA+PFT/CT
L3          2429 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HODGKIN'S DISEASE"+PFT/CT
L5          1420 SEA FILE=HCAPLUS ABB=ON  PLU=ON  TENASCINS+PFT/CT
L10       124493 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MONOCLON?
L12            6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L2 OR L3) AND L5 AND L10



L2         14585 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LYMPHOMA+PFT/CT
L3          2429 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HODGKIN'S DISEASE"+PFT/CT
L13           36 SEA FILE=HCAPLUS ABB=ON  PLU=ON  81C6
L14            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L2 OR L3) AND L13



L2         14585 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LYMPHOMA+PFT/CT
L3          2429 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HODGKIN'S DISEASE"+PFT/CT
L5          1420 SEA FILE=HCAPLUS ABB=ON  PLU=ON  TENASCINS+PFT/CT
L13           36 SEA FILE=HCAPLUS ABB=ON  PLU=ON  81C6
L14            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L2 OR L3) AND L13
L15            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L5 AND L14



L4        394975 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIBODIES/CT OR ANTIBODY OR
                 IMMUNE BODIES
L5          1420 SEA FILE=HCAPLUS ABB=ON  PLU=ON  TENASCINS+PFT/CT
L6        171461 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTITUMOR AGENTS+OLD/CT
L7         14426 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTINEOPLAS? OR ANTICARCINO?
                 OR ONCOLYTIC OR CARCINOSTAT?
L10       124493 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MONOCLON?
L17           34 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4 AND L10 AND L5 AND (L6 OR
                 L7)
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L18          12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND (CYSTIC OR PRETARG?
                OR ADHES? OR ISOFOR? OR MURINE OR ANTI HUMAN OR CHIMER?)/TI



L2        14585 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LYMPHOMA+PFT/CT
L3         2429 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HODGKIN'S DISEASE"+PFT/CT
L4       394975 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIBODIES/CT OR ANTIBODY OR
                IMMUNE BODIES
L5         1420 SEA FILE=HCAPLUS ABB=ON  PLU=ON  TENASCINS+PFT/CT
L6       171461 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTITUMOR AGENTS+OLD/CT
L7        14426 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTINEOPLAS? OR ANTICARCINO?
                OR ONCOLYTIC OR CARCINOSTAT?
L19           8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L2 OR L3) AND L4 AND L5 AND
                (L6 OR L7)


=> s (l12 or l14 or l15 or l18 or l19) not l1   L1 = inventors, previously displayed
           17 RIZZIERI D?/AU
          251 BIGNER D?/AU
          182 ZALUTSKY M?/AU
L73        21 (L12 OR L14 OR L15 OR L18 OR L19) NOT L1

=> file medline; d que l31
FILE 'MEDLINE' ENTERED AT 16:19:43 ON 16 MAR 2004

 FILE LAST UPDATED: 13 MAR 2004 (20040313/UP). FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
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L22        2028 SEA FILE=MEDLINE ABB=ON  PLU=ON  TENASCIN/CT OR TENASCIN OR TN
                RECEPTOR/CN
L23      112078 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTIBODIES, MONOCLONAL+NT/CT
L24      586614 SEA FILE=MEDLINE ABB=ON  PLU=ON  ANTINEOPLASTIC AGENTS+NT/CT
L30           3 SEA FILE=MEDLINE ABB=ON  PLU=ON  L22 AND L23 AND L24
L31           1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L30 AND MULTIFORME/TI


=> file embase; d que 143; d que 149; d que 152
FILE 'EMBASE' ENTERED AT 16:20:03 ON 16 MAR 2004
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 FILE COVERS 1974 TO 11 Mar 2004 (20040311/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
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L34        94332 SEA FILE=EMBASE ABB=ON  PLU=ON  LYMPHOMA+ALL/CT
L35        76699 SEA FILE=EMBASE ABB=ON  PLU=ON  HODGKIN DISEASE+ALL/CT
L36         1686 SEA FILE=EMBASE ABB=ON  PLU=ON  TENASCIN/CT
L38       111423 SEA FILE=EMBASE ABB=ON  PLU=ON  MONOCLONAL ANTIBODY+NT/CT
L42            7 SEA FILE=EMBASE ABB=ON  PLU=ON  (L34 OR L35) AND L36 AND L38
L43            3 SEA FILE=EMBASE ABB=ON  PLU=ON  L42 AND (81C6 OR RADIO?)/TI



L48           10 SEA FILE=EMBASE ABB=ON  PLU=ON  MONOCLONAL ANTIBODY 81C6/CT
L49            6 SEA FILE=EMBASE ABB=ON  PLU=ON  L48 (L) (AE OR CT OR AD OR DO
                 OR DT)/CT



L48           10 SEA FILE=EMBASE ABB=ON  PLU=ON  MONOCLONAL ANTIBODY 81C6/CT
L49            6 SEA FILE=EMBASE ABB=ON  PLU=ON  L48 (L) (AE OR CT OR AD OR DO
                 OR DT)/CT
L51            3 SEA FILE=EMBASE ABB=ON  PLU=ON  MONOCLONAL ANTIBODY 81C6 I
                 131/CT
L52            3 SEA FILE=EMBASE ABB=ON  PLU=ON  L51 NOT L49


=> s l43 or l49 or l52
L74           10 L43 OR L49 OR L52

=> file biosis; d que l60; d que l61
FILE 'BIOSIS' ENTERED AT 16:20:30 ON 16 MAR 2004
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 10 March 2004 (20040310/ED)

FILE RELOADED: 19 October 2003.


L54       104012 SEA FILE=BIOSIS ABB=ON  PLU=ON  HODGKIN? OR ?LYMPHOM?
L55         2553 SEA FILE=BIOSIS ABB=ON  PLU=ON  TENASCIN OR TN RECEPTOR
L56       152428 SEA FILE=BIOSIS ABB=ON  PLU=ON  (ANTIBODY OR ANTIBODIES) (3A)
                 MONOCLONAL
L58           60 SEA FILE=BIOSIS ABB=ON  PLU=ON  81C6
L59            2 SEA FILE=BIOSIS ABB=ON  PLU=ON  L54 AND L55 AND L56
L60            1 SEA FILE=BIOSIS ABB=ON  PLU=ON  L59 AND L58



L55         2553 SEA FILE=BIOSIS ABB=ON  PLU=ON  TENASCIN OR TN RECEPTOR
L56       152428 SEA FILE=BIOSIS ABB=ON  PLU=ON  (ANTIBODY OR ANTIBODIES) (3A)
                 MONOCLONAL
L58           60 SEA FILE=BIOSIS ABB=ON  PLU=ON  81C6
L61           25 SEA FILE=BIOSIS ABB=ON  PLU=ON  L55 AND L56 AND L58

=> s (l60 or l61) not l53   L53 = authors, previously displayed.
L75           24 (L60 OR L61) NOT L53

=> file wpid; d que l68; d que l69; d que l71
```

```
FILE 'WPIDS' ENTERED AT 16:21:10 ON 16 MAR 2004
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FILE LAST UPDATED:          16 MAR 2004      <20040316/UP>
MOST RECENT DERWENT UPDATE:     200418        <200418/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

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    GUIDES, PLEASE VISIT:
    http://thomsonderwent.com/support/userguides/              <<<

>>> ADDITIONAL POLYMER INDEXING CODES WILL BE IMPLEMENTED FROM
    DERWENT UPDATE 200403.
    THE TIME RANGE CODE WILL ALSO CHANGE FROM 018 TO 2004.
    SDIS USING THE TIME RANGE CODE WILL NEED TO BE UPDATED.
    FOR FURTHER DETAILS: http://thomsonderwent.com/chem/polymers/ <<<


L67             4 SEA FILE=WPIDS ABB=ON  PLU=ON  81C6
L68             3 SEA FILE=WPIDS ABB=ON  PLU=ON  L67 NOT METHYLPIPER?/TI


L63          4935 SEA FILE=WPIDS ABB=ON  PLU=ON  HODGKIN? OR ?LYMPHOM?
L64           108 SEA FILE=WPIDS ABB=ON  PLU=ON  TENASCIN OR TN RECEPTOR
L65         15615 SEA FILE=WPIDS ABB=ON  PLU=ON  (ANTIBODY OR ANTIBODIES) (3A)
                  MONOCLONAL
L69             7 SEA FILE=WPIDS ABB=ON  PLU=ON  L63 AND L64 AND L65


L64           108 SEA FILE=WPIDS ABB=ON  PLU=ON  TENASCIN OR TN RECEPTOR
L65         15615 SEA FILE=WPIDS ABB=ON  PLU=ON  (ANTIBODY OR ANTIBODIES) (3A)
                  MONOCLONAL
L66         16878 SEA FILE=WPIDS ABB=ON  PLU=ON  ANTITUM? OR ANTINEOPLAST? OR
                  ANTICARCINO? OR ONCOLYTIC OR CARCINOSTAT? OR ANTI (W) (TUMOR?
                  OR TUMOUR? OR CARCINOGEN? OR NEOPLAS?)
L70             3 SEA FILE=WPIDS ABB=ON  PLU=ON  L64 AND L65 AND L66
L71             2 SEA FILE=WPIDS ABB=ON  PLU=ON  L70 NOT OSTEOIMP?/TI

=> s (168 or 169 or 171) not 162   L62 = authors, previously displayed
L76             8 (L68 OR L69 OR L71) NOT L62

=> dup rem l31 l73 l74 l75 l76
FILE 'MEDLINE' ENTERED AT 16:22:14 ON 16 MAR 2004

FILE 'HCAPLUS' ENTERED AT 16:22:14 ON 16 MAR 2004
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FILE 'EMBASE' ENTERED AT 16:22:14 ON 16 MAR 2004

FILE 'BIOSIS' ENTERED AT 16:22:14 ON 16 MAR 2004

FILE 'WPIDS' ENTERED AT 16:22:14 ON 16 MAR 2004

PROCESSING COMPLETED FOR L31
PROCESSING COMPLETED FOR L73
PROCESSING COMPLETED FOR L74
PROCESSING COMPLETED FOR L75
PROCESSING COMPLETED FOR L76
L77 56 DUP REM L31 L73 L74 L75 L76 (8 DUPLICATES REMOVED)
ANSWER '1' FROM FILE MEDLINE
ANSWERS '2-22' FROM FILE HCAPLUS
ANSWERS '23-31' FROM FILE EMBASE
ANSWERS '32-54' FROM FILE BIOSIS
ANSWERS '55-56' FROM FILE WPIDS

=> d ibib ab l77 1-56

L77 ANSWER 1 OF 56 MEDLINE on STN
ACCESSION NUMBER: 2002372501 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12118034
TITLE: Treatment of newly diagnosed glioblastoma **multiforme**.
COMMENT: Comment on: J Clin Oncol. 2001 Jan 15;19(2):509-18. PubMed ID: 11208845
Comment on: J Clin Oncol. 2002 Mar 1;20(5):1375-82. PubMed ID: 11870182
Comment on: J Clin Oncol. 2002 Mar 1;20(5):1389-97. PubMed ID: 11870184
AUTHOR: Nieder Carsten
SOURCE: Journal of clinical oncology : official journal of the American Society of Clinical Oncology, (2002 Jul 15) 20 (14) 3179-80; author reply 3181-2.
Journal code: 8309333. ISSN: 0732-183X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020716
Last Updated on STN: 20030111
Entered Medline: 20020808

L77 ANSWER 2 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:2624 HCAPLUS
DOCUMENT NUMBER: 140:55677
TITLE: Anti-tenascin **antibody** fragments and minibodies for treatment of lymphoma
INVENTOR(S): Bigner, Darrell; Zalutsky, Michael; Kuan, Chien-Tsun
PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000216	A2	20031231	WO 2003-US19268	20030619

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-390864P P 20020621

AB The authors disclose treatment of lymphoma comprising administering **antibody** fragments, minibodies, or mixts. thereof that bind to tenascin in a therapeutically effective amount Preferably the **antibody** fragment is a fragment of **monoclonal antibody 81C6** or an **antibody** that binds to the epitope bound by **monoclonal antibody 81C6**. Preferably the **antibody** fragment is labeled with or conjugated to a chemotherapeutic agent, particularly a radioisotope such as 131I.

L77 ANSWER 3 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2003:719519 HCAPLUS
DOCUMENT NUMBER: 139:259963
TITLE: Anti-CD74 **antibodies** and conjugates for diagnosis and treatment of immune and autoimmune diseases, infections and cancers
INVENTOR(S): Hansen, Hans; Leung, Shui-on; Qu, Zhengxing; Goldenberg, David M.
PATENT ASSIGNEE(S): Immunomedics, Inc., USA; McCall, John Douglas
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074567	A2	20030912	WO 2003-GB890	20030303
WO 2003074567	A3	20031231		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-360259P P 20020301

AB The present invention provides humanized, chimeric and human anti-CD74

antibodies, CD74 **antibody** fusion proteins, immunoconjugates, vaccines and bispecific that bind to CD74, the major histocompatibility complex (MHC) class-II invariant chain, Ii, which is useful for the treatment and diagnosis of B-cell disorders, such as B-cell malignancies, other malignancies in which the cells are reactive with CD74, and autoimmune diseases, and methods of treatment and diagnosis.

L77 ANSWER 4 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2003:696922 HCAPLUS
DOCUMENT NUMBER: 139:229262
TITLE: **Anti-human** tenascin **monoclonal antibody**
INVENTOR(S): De Santis, Rita; Anastasi, Anna Maria
PATENT ASSIGNEE(S): Sigma-Tau Industrie Farmaceutiche Riunite, S.p.A., Italy
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072608	A1	20030904	WO 2003-IT98	20030220

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004005643	A1	20040108	US 2003-372719	20030225

PRIORITY APPLN. INFO.: US 2002-359299P P 20020226
AB A novel anti-human tenascin ST2146 **monoclonal antibody** is described endowed with high affinity with the native antigen and high tumor selectivity. The cST2146 hybridoma is stably producing the **antibody** in high d. culture conditions and is suitable for the industrial development of ST2146-based products. ST2146 exhibits properties exploitable for both therapeutic and diagnostic applications.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 5 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2003:656808 HCAPLUS
DOCUMENT NUMBER: 139:196278
TITLE: Anti-CD20 antibodies and fusion proteins for diagnosis and treatment of B cell disease, B cell malignancy and autoimmune diseases
INVENTOR(S): Hansen, Hans; Qu, Zhengxing; Goldenberg, David M.
PATENT ASSIGNEE(S): Immunomedics, Inc., USA; McCall, John Douglas
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068821	A2	20030821	WO 2003-GB665	20030214
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003219433	A1	20031127	US 2003-366709	20030214
PRIORITY APPLN. INFO.:			US 2002-356132P P	20020214
			US 2002-416232P P	20021007

AB The present invention provides humanized, chimeric and human anti-CD20 antibodies and CD20 antibody fusion proteins that bind to a human B cell marker, referred to as CD20, which is useful for the treatment and diagnosis of B-cell disorders, such as B-cell malignancies and autoimmune diseases, and methods of treatment and diagnosis.

L77 ANSWER 6 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2003:320021 HCAPLUS
DOCUMENT NUMBER: 138:336427
TITLE: Direct targeting binding multivalent monospecific proteins of human
INVENTOR(S): Rossi, Edmund; Chang, Chien-Hsing Ken; Goldenberg, David M.
PATENT ASSIGNEE(S): IBC Pharmaceuticals, USA; Immunomedics Inc.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003033654	A2	20030424	WO 2002-US32718	20021015
WO 2003033654	A3	20031113		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003148409	A1	20030807	US 2002-270073	20021015
PRIORITY APPLN. INFO.:			US 2001-328835P P	20011015
			US 2001-341881P P	20011221
			US 2002-345641P P	20020108
			US 2002-404919P P	20020822

AB The present invention relates to multivalent, monospecific binding proteins. These binding proteins comprise two or more binding sites, where each binding site specifically binds to the same type of target cell, and preferably with the same antigen on such a target cell. The present invention further relates to compns. of monospecific diabodies, triabodies, and tetrabodies, and to recombinant vectors useful for the expression of these functional binding proteins in a microbial host. Also provided are methods of using invention compns. in the treatment and/or diagnosis of tumors.

L77 ANSWER 7 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 2002:241597 HCAPLUS
DOCUMENT NUMBER: 136:352096
TITLE: Phase II trial of **murine** 131I-labeled antitenascin **monoclonal antibody** 81C6 administered into surgically created resection cavities of patients with newly diagnosed malignant gliomas
AUTHOR(S): Reardon, David A.; Akabani, Gamal; Coleman, R. Edward; Friedman, Allan H.; Friedman, Henry S.; Herndon, James E., II; Cokgor, Ilkcan; McLendon, Roger E.; Pegram, Charles N.; Provenzale, James M.; Quinn, Jennifer A.; Rich, Jeremy N.; Regalado, Lorna V.; Sampson, John H.; Shafman, Timothy D.; Wikstrand, Carol J.; Wong, Terence Z.; Zaho, Xiao-Guang; Zalutsky, Michael R.; Bigner, Darell D.
CORPORATE SOURCE: Departments of Surgery, Medicine, Pathology, Radiology, and Biostatistics and Bioinformatics, Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Journal of Clinical Oncology (2002), 20(5), 1389-1397
CODEN: JCONDN; ISSN: 0732-183X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of this study was to assess the efficacy and toxicity of intraresection cavity 131I-labeled murine antitenascin **monoclonal antibody** 81C6 and determine its true response rate among patients with newly diagnosed malignant glioma. In this phase II trial, 120 mCi of 131I-labeled murine 81C6 was injected directly into the surgically created resection cavity of 33 patients with previously untreated malignant glioma (glioblastoma multiforme [GBM], n = 27; anaplastic astrocytoma, n = 4; anaplastic oligodendroglioma, n = 2). Patients then received conventional external-beam radiotherapy followed by a year of alkylator-based chemotherapy. Median survival for all patients and those with GBM was 86.7 and 79.4 wk, resp. Eleven patients remain alive at a median follow-up of 93 wk (range, 49 to 220 wk). Nine patients (27%) developed reversible hematol. toxicity, and histol. confirmed, treatment-related neurol. toxicity occurred in five patients (15%). One patient (3%) required reoperation for radionecrosis. Median survival achieved with 131I-labeled 81C6 exceeds that of historical controls treated with conventional radiotherapy and chemotherapy, even after accounting for established prognostic factors including age and Karnofsky performance status. The median survival achieved with 131I-labeled 81C6 compares favorably with either 125I interstitial brachytherapy or stereotactic radiosurgery and is associated with a significantly lower rate of reoperation for radionecrosis. Our results confirm the efficacy of 131I-labeled 81C6 for patients with newly diagnosed malignant glioma and suggest that a randomized phase III study is indicated.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 8 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 1995:294069 HCAPLUS
DOCUMENT NUMBER: 122:282221
TITLE: Treatment of **cystic** tumors with an **antibody** binding to tenascin
INVENTOR(S): Bigner, Darell D.; Zalutsky, Michael
PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9421293	A1	19940929	WO 1994-US2703	19940314
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9464458	A1	19941011	AU 1994-64458	19940314
US 5624659	A	19970429	US 1995-392419	19950222

PRIORITY APPLN. INFO.: US 1993-33827 19930319
WO 1994-US2703 19940314

AB Methods of treating solid and cystic tumors are disclosed. The method comprises administering to a subject afflicted with a cystic tumor an **antibody** which binds to tenascin in a therapeutically effective amount The administering step is carried out by depositing the **antibody** in the cyst cavity of the cystic tumor. For solid tumors, disclosed is a method involving first, removing a solid tumor from a solid tissue organ of an afflicted subject; then forming an enclosed resection cavity in the organ of the subject at the location from which the solid tumor was removed; and then administering to the subject an **antineoplastic** agent by depositing the **antineoplastic** agent in the resection cavity. Particularly preferred for carrying out the foregoing is the **monoclonal antibody** 81C6 and **antibodies** which bind to the epitope bound by **monoclonal antibody** 81C6. Cystic glioblastoma or astrocytoma patients treated as described with 81C6-iodine-131 conjugate survived longer than those treated by alternate techniques. A chimeric mouse-human **antibody** cross-reactive with 81C6 was also prepared and tested.

L77 ANSWER 9 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 1995:27087 HCAPLUS
DOCUMENT NUMBER: 122:7477
TITLE: Generation and characterization of a mouse/human **chimeric antibody** directed against extracellular matrix protein tenascin
AUTHOR(S): He, Xuanmin; Archer, Gary E.; Wikstrand, Carol J.; Morrison, Sherie L.; Zalutsky, Michael R.; Bigner, Darell D.; Batra, Surinder K.
CORPORATE SOURCE: Department of Pathology, Duke University Medical Center, Box 3156, Durham, NC, 27710, USA
SOURCE: Journal of Neuroimmunology (1994), 52(2), 127-37
CODEN: JNRIDW; ISSN: 0165-5728
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The murine anti-tenascin **monoclonal antibody** 81C6, following iodination, has been shown to be an efficient localizing and therapeutic agent in both s.c. and intracranial human glioma xenograft

models in athymic mice and rats. Similarly, effective **monoclonal antibody** 81C6 localization has been demonstrated in glioma patients, and Phase I trials with the intact murine IgG2b κ mol. are currently in progress. In order to maximize the potential for repeated administration by minimizing murine Fc-mediated immunogenicity and reducing Fc-mediated immune effects, we created murine 81C6 variable region/human IgG2 chimeric **monoclonal antibodies** by the mol. cloning of the variable region genes of mouse 81C6 and their genetic linkage to human constant region exons. The resulting chimeric constructs were introduced into SP2/0 cells, and stable transfectomas were selected by G418 and mycophenolic acid resistance. The resistant clones were screened for anti-tenascin activity on tenascin-coated plates by ELISA. The N-terminal amino acid sequence of both heavy and light chains of the purified chimeric 81C6 **antibody** matched exactly with that of the native mouse 81C6 as well as with that deduced from the nucleotide sequence. The production level of chimeric 81C6 (13.9 mg/mL) from ascites in the highest expressing transfectoma was much higher than that of native mouse 81C6 (2.5 mg/mL). The chimeric **antibody** showed the same specificity and equivalent affinity for human intact tenascin or tenascin-expressing cells as the native mouse 81C6 **antibody**. Direct comparison of radioiodinated chimeric and radioiodinated mouse 81C6 biodistribution in s.c. and intracranial xenograft-bearing mice showed higher tumor-to-normal tissue ratios for chimeric 81C6 as compared with native mouse 81C6. The improved localizing and clearance characteristics of chimeric 81C6 in xenograft model systems suggests that chimeric 81C6 would be an improved reagent for intracompartmental therapy of tenascin-expressing tumors in the human central nervous system.

L77 ANSWER 10 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:120888 HCAPLUS
TITLE: **Chimeric** and humanized ant-α-fetoprotein **antibodies** Immu31 and fragments for diagnosis and therapy of hepatocellular carcinoma, hepatoblastoma and germ cell tumors
INVENTOR(S): Hansen, Hans; Qu, Zhengxing; Goldenberg, David M.
PATENT ASSIGNEE(S): Immunomedics, Inc., USA; McCall, John Douglas
SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004013180	A2	20040212	WO 2003-GB3325	20030801

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-399707P P 20020801
AB The present invention provides humanized, chimeric and human anti-alpha-fetoprotein **antibodies**, fusion proteins, and

fragments thereof. The **antibodies**, fusion proteins, and fragments thereof, as well as combinations with other suitable **antibodies**, are useful for the treatment and diagnosis of hepatocellular carcinoma, hepatoblastoma, germ cell tumors, carcinoma and other AFP-producing tumors.

L77 ANSWER 11 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:1007015 HCAPLUS
DOCUMENT NUMBER: 140:58438
TITLE: **Monoclonal** anti-MUC1 **antibody** PAM4 and **chimeric antibodies** for diagnosis and therapy of pancreatic cancer
INVENTOR(S): Gold, David V.; Goldenberg, David M.; Hansen, Hans
PATENT ASSIGNEE(S): Immunomedics, Inc., USA; McCall, John Douglas
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003106497	A1	20031224	WO 2003-GB2585	20030616

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-388313P P 20020614
AB This invention relates to monovalent and multivalent, monospecific **antibodies** and to monovalent and multivalent, multispecific **antibodies**. One embodiment of these **antibodies** has one or more identical binding sites where each binding site binds with a target antigen or an epitope on a target antigen. Another embodiment of these **antibodies** has two or more binding sites where these binding sites have affinity towards different epitopes on a target antigen or different target antigens, or have affinity towards a target antigen and a hapten. The present invention further relates to recombinant vectors useful for the expression of these functional **antibodies** in a host. More specifically, the present invention relates to the tumor-associated **antibody** designated PAM4. The invention further relates to chimeric PAM4 **antibodies**, and the use of such **antibodies** in diagnosis and therapy.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 12 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:777842 HCAPLUS
DOCUMENT NUMBER: 139:290593
TITLE: A tumor-specific tenascin **isoform**, tenascin W, and its use in the diagnosis and treatment of cancer
INVENTOR(S): Chiquet-Ehrismann, Ruth; Scherberich, Arnaud

PATENT ASSIGNEE(S): Novartis Forschungsstiftung, Zweigniederlassung Friedrich Miescher Institute for Biomedical Research, Switz.
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080663	A2	20031002	WO 2003-EP3150	20030326

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-7224 A 20020327

AB Tenascin-W, an extracellular matrix mol. that is abundant in metastatic tumors, but not in non-metastatic tumors, is identified and a cDNA encoding it is cloned. A system comprising a sample expressing tenascin-W is used as an in vitro method for screening possible anti-tumor agents or for agents that promote osteogenesis. A mouse cDNA for the protein was cloned using primers derived from tenascin R and this was used to identify a cDNA for human tenascin W. Tenascin W has the protein motifs and organization typical of a tenascin. The protein is found in the developing mouse embryo and in metastatic tumors, but not in non-metastatic tumors.

L77 ANSWER 13 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:737609 HCAPLUS
DOCUMENT NUMBER: 139:240352
TITLE: Avidin dimers effective in increasing the concentration of radioactive biotin in **pretargeted** radioimmunotherapy
INVENTOR(S): De Santis, Rita; Lindstedt, Ragnar; Nuzzolo, Carlo Antonio
PATENT ASSIGNEE(S): Sigma-Tau Industrie Farmaceutiche Riunite S.p.A., Italy
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003075960	A1	20030918	WO 2003-IT135	20030306

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,

UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IT 2002-RM128 A 20020308

AB Dimers of avidin and streptavidins (diavidins) are described wherein the linker is suberate, which in turn, is bound to different functional groups (-NH2 o-COOH) of avidin. As compared to avidin, the diavidins have shown the ability to increase the amount of labeled biotin on the target, when used in an in vitro pretargeting test using supported human tenascin, the biotinylated anti-tenascin **monoclonal antibody** (Mab-B), avidin/diavidin, and biotin-3H. The use of such diavidins is also described in cancer diagnosis and anticancer therapy based on the three-step pretargeted radioimmunotherapy procedure.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 14 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:719518 HCAPLUS
DOCUMENT NUMBER: 139:259962
TITLE: Humanized **murine** anti-epithelial glycoprotein 1 (EGP-1) **antibodies** RS7 and conjugates for diagnosis and treatment of cancer
INVENTOR(S): Govindan, Serengulam; Qu, Zhengxing; Hansen, Hans J.; Goldenberg, David M.
PATENT ASSIGNEE(S): Immunomedics, Inc., USA; Mccall, John Douglas
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074566	A2	20030912	WO 2003-GB885	20030303

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004001825	A1	20040101	US 2003-377121	20030303

PRIORITY APPLN. INFO.: US 2002-360229P P 20020301

AB This invention relates to monovalent and multivalent, monospecific binding proteins and to multivalent, multispecific binding proteins. One embodiment of these binding proteins has one or more binding sites where each binding site binds with a target antigen or an epitope on a target antigen. Another embodiment of these binding proteins has two or more binding sites where each binding site has affinity towards different epitopes on a target antigen or has affinity towards either a target antigen or a hapten. The present invention further relates to recombinant vectors useful for the expression of these functional binding proteins in

a host. More specifically, the present invention relates to the tumor-associated antigen binding protein designated RS7, and other EGP-1 binding-proteins. The invention further relates to humanized, human and chimeric RS7 antigen binding proteins, and the use of such binding proteins in diagnosis and therapy.

L77 ANSWER 15 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:472615 HCAPLUS
DOCUMENT NUMBER: 139:30800
TITLE: Streptavidin expressed gene fusions with single-chain **antibodies** and their use as targeting vehicles for diagnosis and treatment of cancer
INVENTOR(S): Goshorn, Stephen Charles; Graves, Scott Stoll; Schultz, Joanne Elaine; Lin, Yukang; Sanderson, James Allen; Reno, John M.; Dearstyne, Erica A.
PATENT ASSIGNEE(S): Neorx Corporation, USA
SOURCE: PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003050260	A2	20030619	WO 2002-US39429	20021206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003095977	A1	20030522	US 2001-13173	20011207
US 2003103948	A1	20030605	US 2002-150762	20020517
US 2003143233	A1	20030731	US 2002-244821	20020916

PRIORITY APPLN. INFO.:
US 2001-13173 A 20011207
US 2002-150762 A 20020517
US 2002-244821 A 20020916
US 1999-137900P P 19990607
US 1999-168976P P 19991203
US 2000-589870 A2 20000605

AB The present invention provides vectors for expressing genomic streptavidin fusion cassettes. In the various embodiments, fusion proteins produced from these vectors are provided. In particular embodiments, fusion proteins comprising a single-chain **antibody** and genomic streptavidin are provided as are vectors encoding the same. The single-chain **antibodies** are directed to cell surface antigens, or cell-associated stromal or matrix antigens, including, but not limited to, CD20, CD22, CD25, CD45, CD52, CD56, CD57, EGP40 (or EPCAM or KSA), N-CAM, CEA, TAG-72, γ-glutamyl transferase, mucins (MUC1 through MUC7), human β-chorionic gonadotropin, EGF receptor, interleukin-2 receptor, her2/neu, Lewis Y, gangliosides GD2 and GM2, tenascin, sialylated tenascin, somatostatin, activated tumor stromal antigen, or neoangiogenic antigens. Generically, a single-chain Fv/streptavidin (scFvSA) fusion protein is expressed from the genetic fusion of the single-chain

antibody of the variable regions to the genomic streptavidin of Streptomyces avidinii. The scFv gene consists of the variable regions of the light and heavy chains separated by a DNA linker sequence. The streptavidin coding sequence is joined to the 3'-terminus of the scFv gene, and the two genes are separated in-frame by a second DNA linker sequence. The signal sequence from the streptavidin gene is fused at the 5'-terminus of the scFvSA gene to direct expression to the Escherichia coli periplasmic space. The scFvSA gene is under control of the lac promoter, and the expressed fusion protein is extracted and purified from E. coli and forms a soluble tetramer of .apprx.173,000 mol. weight Also provided, are methods of using the fusion proteins of the present invention, in the absence and presence of a radiation-sensitizing agent (e.g., Gemcitabine), and in particular, the use of scFvSA fusion proteins as diagnostic markers or as cell-specific targeting agents.

L77 ANSWER 16 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:590597 HCAPLUS
DOCUMENT NUMBER: 139:144951
TITLE: Preparation of fusion genes encoding streptavidin and single chain **antibody** and methods of therapeutic use thereof
INVENTOR(S): Goshorn, Stephen Charles; Graves, Scott Stoll; Schultz, Joanne Elaine; Lin, Yukang; Sanderson, James Allen; Reno, John M.; Dearstyne, Erica A.
PATENT ASSIGNEE(S): NeoRx Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 89 pp., Cont.-in-part of U.S. Ser. No. 150,762.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003143233	A1	20030731	US 2002-244821	20020916
US 2003095977	A1	20030522	US 2001-13173	20011207
US 2003103948	A1	20030605	US 2002-150762	20020517
WO 2003050260	A2	20030619	WO 2002-US39429	20021206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 1999-137900P	P	19990607
US 1999-168976P	P	19991203
US 2000-589870	A2	20000605
US 2001-13173	A2	20011207
US 2002-150762	A2	20020517
US 2002-244821	A	20020916

AB The present invention provides vectors for expressing genomic streptavidin fusion cassettes and therapeutic uses. In the various embodiments, fusion proteins produced from these vectors are provided. In particular embodiments, fusion proteins comprising a single chain **antibody**

and genomic streptavidin are provided as are vectors encoding the same. Also provided, are methods of using the fusion proteins of the present invention, in the absence and presence of a radiation-sensitizing agent, and in particular, the use of scFvSA fusion proteins as diagnostic markers or as a cell specific targeting agents.

L77 ANSWER 17 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:435061 HCAPLUS
DOCUMENT NUMBER: 139:21033
TITLE: Vectors expressing soluble form of single chain **antibody** and streptavidin (scFvSA) fusions and uses thereof as diagnostic markers or as cell specific targeting agents
INVENTOR(S): Goshorn, Stephen Charles; Graves, Scott Stoll; Schultz, Joanne Elaine; Lin, Yukang; Sanderson, James Allen; Reno, John M.; Dearstyne, Erica A.
PATENT ASSIGNEE(S): NeoRx Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 84 pp., Cont.-in-part of U.S. Ser. No. 13,173.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003103948	A1	20030605	US 2002-150762	20020517
US 2003095977	A1	20030522	US 2001-13173	20011207
US 2003143233	A1	20030731	US 2002-244821	20020916
WO 2003050260	A2	20030619	WO 2002-US39429	20021206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 1999-137900P	P	19990607
US 1999-168976P	P	19991203
US 2000-589870	A2	20000605
US 2001-13173	A2	20011207
US 2002-150762	A2	20020517
US 2002-244821	A	20020916

AB The present invention provides vectors for expressing Streptomyces avidinii genomic streptavidin (SA) fusion cassettes. A genomic streptavidin expressed gene fusion is expressed as a soluble protein into the periplasmic space of bacteria and undergoes spontaneous folding. Such expression offers the advantage that the periplasm is a low biotin environment and one need not purify and refold the protein under harsh denaturing conditions that may prove fatal to the polypeptide encoded by a heterologous nucleic acid mol. fused to the genomic streptavidin nucleic acid mol. In the various embodiments, fusion proteins produced from these vectors are provided. In particular embodiments, fusion proteins comprising a single chain **antibody** and streptavidin (scFvSA) are provided as are vectors encoding the same. The single chain

antibodies are directed to cell surface antigens or cell-associated stromal or matrix proteins such as CD20, CD45, CD22, CD52, CD56, CD57, EGP40, NCAM, CEA, TAG-72, mucins (MUC1-7), 13HCG, EGF receptor, IL-2 receptor, her2/neu, Lewis Y, GD2, GM2, tenascin, sialylated tenascin, somatostatin, activated tumor stromal antigen or neoangiogenic antigens. Also provided, are methods of using the fusion proteins of the present invention, in the absence and presence of a radiation-sensitizing agent, and in particular, the use of scFvSA fusion proteins as diagnostic markers or as a cell specific targeting agents.

L77 ANSWER 18 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:396269 HCAPLUS
DOCUMENT NUMBER: 138:400405
TITLE: Streptavidin-**antibody** fusion proteins for diagnosis and specific cell targeting
INVENTOR(S): Goshorn, Stephen Charles; Graves, Scott Stoll; Schultz, Joanne Elaine; Lin, Yukang; Sanderson, James Allen; Reno, John M.
PATENT ASSIGNEE(S): Neorx Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 72 pp., Cont.-in-part of U.S. Ser. No. 589,870
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003095977	A1	20030522	US 2001-13173	20011207
US 2003103948	A1	20030605	US 2002-150762	20020517
US 2003143233	A1	20030731	US 2002-244821	20020916
WO 2003050260	A2	20030619	WO 2002-US39429	20021206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 1999-137900P P 19990607
US 1999-168976P P 19991203
US 2000-589870 A2 20000605
US 2001-13173 A2 20011207
US 2002-150762 A2 20020517
US 2002-244821 A 20020916

AB The present invention provides vectors for expressing genomic streptavidin fusion cassettes and fusion protein produced from the vectors. In particular embodiments, fusion proteins comprising a single chain **antibody** and genomic streptavidin are provided as are vectors encoding the same. Also provided are methods of using the fusion proteins of the present invention, and in particular, the use of scFvSA fusion proteins as diagnostic markers or as a cell specific targeting agents. The single chain **antibodies** are directed to cell surface antigens or cell-associated stromal or matrix protein such as CD20, CD45, CD22, CD52, CD56, CD57, EGP40, NCAM, CEA, TAG-72, mucins (MUC1-7), 13HCG,

EGF receptor, IL-2 receptor, her2/neu, Lewis Y, GD2, GM2, tenascin, sialylated tenascin, somatostatin, activated tumor stromal antigen or neoangiogenic antigens.

L77 ANSWER 19 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:252240 HCAPLUS
DOCUMENT NUMBER: 139:399507
TITLE: Novel antitenascin **antibody** with increased tumour localisation for **Pretargeted** **Antibody**-Guided RadioImmunoTherapy (PAGRITR)
AUTHOR(S): De Santis, R.; Anastasi, A. M.; D'Alessio, V.; Pelliccia, A.; Albertoni, C.; Rosi, A.; Leoni, B.; Lindstedt, R.; Petronzelli, F.; Dani, M.; Verdoliva, A.; Ippolito, A.; Campanile, N.; Manfredi, V.; Esposito, A.; Cassani, G.; Chinol, M.; Paganelli, G.; Carminati, P.
CORPORATE SOURCE: Immunology Department, Sigma Tau SpA R&D, Rome, Italy
SOURCE: British Journal of Cancer (2003), 88(7), 996-1003
CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Pretargeted **Antibody**-Guided RadioImmunoTherapy (PAGRIT) method is based on i.v., sequential administration of a biotinylated **antibody**, avidin/streptavidin and 90Y-labeled biotin. The hybridoma clone producing the **monoclonal** antitenascin **antibody** BC4, previously used for clin. applications, was found not suitable for further development because of the production of an addnl., nonfunctional light chain. In order to solve this problem, the new cST2146 hybridoma clone was generated. The **monoclonal** **antibody** ST2146, produced by this hybridoma, having the same specificity as BC4 but lacking the nonfunctional light chain, was characterized. ST2146 was found able to bind human tenascin at an epitope strictly related, if not identical, to the antigenic epitope of BC4. It showed, compared to BC4, higher affinity and immunoreactivity and similar selectivity by immunohistochem. Biodistribution studies of biotinylated ST2146 and three other **monoclonal** antitenascin **antibodies** showed for ST2146 the highest and more specific tumor localisation in HT29-grafted nude mice. On the overall, ST2146 appears to be a good alternative to BC4 for further clin. development of PAGRIT.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 20 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:881321 HCAPLUS
DOCUMENT NUMBER: 134:38630
TITLE: Streptavidin expressed gene fusions forming tetrameric complexes with therapeutic implications for adenocarcinomas and hematol. malignancies
INVENTOR(S): Goshorn, Stephen Charles; Graves, Scott Stoll; Schultz, Joanne Elaine; Lin, Yukang; Sanderson, James Allen; Reno, John M.
PATENT ASSIGNEE(S): Neorx Corp., USA
SOURCE: PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075333	A1	20001214	WO 2000-US15595	20000605
WO 2000075333	C2	20020620		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1190061	A1	20020327	EP 2000-941246	20000605

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

JP 2003501096	T2	20030114	JP 2001-502595	20000605

PRIORITY APPLN. INFO.:	US 1999-137900P	P	19990607
	US 1999-168976P	P	19991203
	WO 2000-US15595	W	20000605

AB The present invention provides vectors for expressing genomic streptavidin fusion cassettes which include inducible promoters and various linkers and signal sequences. In the various embodiments, fusion proteins produced from these vectors are provided. In particular embodiments, fusion proteins comprising a single chain **antibody** (huNR-LU-10) and genomic streptavidin are provided as are vectors encoding the same. Also provided, are methods of using the fusion proteins of the present invention, and in particular, the use of scFvSA fusion proteins involving B9E9 as diagnostic markers or as a cell specific targeting agents. In addition tetravalent **antibodies** that contact a fusion protin forming a tetrametric complex which may comprise a tumor cell surface-associated protein and a streptavidin portion capable of binding biotin and a biotinylated radionuclide containing compound A immunoreactivity assay is described in addition to monitoring of blood clearance and tumor uptake of fusion proteins. Some adenocarcinomas and hematol. malignancies such as non-Hodgkin's lymphoma may be treated with these fusio-protein expressing vectors. This system offers the expression of a genomic streptavidin gene fusion as a soluble protein into the periplasmic space of Escherichia coli where it undergoes spontaneous folding. This expression offers efficient protein folding where one does not need to purify and refold the protein expressed.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 21 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:505353 HCAPLUS

DOCUMENT NUMBER: 121:105353

TITLE: Tenascin **isoforms**: Possible targets for diagnosis and therapy of cancer and mechanisms regulating their expression

AUTHOR(S): Leprini, Alessandra; Querze, Germano; Zardi, Luciano

CORPORATE SOURCE: Lab. Cell Biol., Ist. Naz. per la Ric. sul Cancro, Genoa, 16132, Italy

SOURCE: Perspectives on Developmental Neurobiology (1994), 2(1), 117-23
CODEN: PDENED; ISSN: 1064-0517

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review, with 50 refs. Functionally different tenascin (TN) isoforms containing varying nos. of type III homol. repeats are generated by

alternative splicing of a single TN primary transcript. It has recently been reported that the larger TN isoform is, in general, more expressed in neoplastic tissues than in the normal tissues from which the tumor originates. This is due, at least in breast lesions, to the high proliferative activity of stromal elements. In fact, TN splicing is cell-cycle dependent, thus offering a viable system to study the mol. mechanisms that regulate alternative splicing and suggesting that cell-cycle dependent modifications in the splicing pattern of primary transcripts (which very likely are not limited to the TN pre-mRNA) may also be a cell-cycle regulatory mechanism. Furthermore, the very high accumulation of the larger TN isoform in neoplasia allows wider diagnostic and therapeutic **monoclonal antibodies** specific for the larger TN isoforms be considered for a number of tumors.

L77 ANSWER 22 OF 56 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:537319 HCAPLUS
DOCUMENT NUMBER: 119:137319
TITLE: **Monoclonal antibodies** (Mabs) to human tenascin cell **adhesion**-associated domain
INVENTOR(S): Kawakatsu, Hisatetsu; Yano, Junichi
PATENT ASSIGNEE(S): Nippon Shinyaku Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05111390	A2	19930507	JP 1991-302472	19911021

PRIORITY APPLN. INFO.: JP 1991-302472 19911021

AB Mabs to the human tenascin cell adhesion-associated domain are prepared by the hybridoma method. The Mabs are useful for inhibition of metastasis of tumors. A synthetic peptide (27 amino acids) containing the cell adhesion-associated domain of tenascin was conjugated with keyhole limpet hemocyanin for immunizing Balb/c male mice. The spleen cells of the immunized mice were fused with 8-azaguanine-resistant mouse myeloma SP2/0-Ag14 cells; after screening by ELISA, hybridomas producing the Mabs were obtained, cloned, and introduced into the abdominal cavity for production of the Mabs by the ascites method. The Mabs inhibited the adhesion of tenascin to HBL100 cells.

L77 ANSWER 23 OF 56 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003005970 EMBASE
TITLE: Clinical immunotherapy for brain tumors.
AUTHOR: Fecci P.E.; Sampson J.H.
CORPORATE SOURCE: Dr. J.H. Sampson, Department of Neurosurgery, Duke University Medical Center, Durham, NC 27710, United States. samps001@mc.duke.edu
SOURCE: Neuroimaging Clinics of North America, (2002) 12/4 (641-664).
Refs: 192
ISSN: 1052-5149 CODEN: NCNAEO
PUBLISHER IDENT.: S 1052-5149(02)00027-8
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery

023 Nuclear Medicine
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English
SUMMARY LANGUAGE: English

AB As an immunization platform for brain tumors, dendritic cells supply an impressive host of advantages. On the simplest level, they provide the safety and tumor-specificity so wanted by current therapeutic options. Yet, in addition, as the fundamental antigen-presenting cell, they circumvent many of the immunologic challenges that gliomas and the CNS proffer and that other immunotherapeutic modes fail to overcome. Directions to take now include the identification of new tumor-specific and tumor-associated antigens; the determination of the optimal dendritic cell subtype, generation, loading method, maturation state, dose, and route of delivery for immunizations; the further characterization of dendritic cells and their activities; and, potentially, the discovery of ways to pulse dendritic cells efficiently in vivo. Preclinical studies continue to play an important role in refining this form of active immunotherapy.

L77 ANSWER 24 OF 56 EMBASE
on STN

ACCESSION NUMBER: 2002095198 EMBASE
TITLE: Clinical trial design and scoring of radionuclide therapy endpoints: Normal organ toxicity and tumor response.
AUTHOR: Meredith R.
CORPORATE SOURCE: Dr. R. Meredith, University of Alabama, Department of Radiation Oncology, WTI T117, 1824 6th Ave. South, Birmingham, AL 35233-1932, United States
SOURCE: Cancer Biotherapy and Radiopharmaceuticals, (2002) 17/1 (83-99).
Refs: 112
ISSN: 1084-9785 CODEN: CBRAFJ
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 014 Radiology
023 Nuclear Medicine
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Like other cancer therapy agents under development, radionuclide therapies are usually evaluated in a progressive series of clinical trials after basic science, human cell culture and animal model studies. Toxicities during these trials are graded using common scoring systems that are in widespread use such as the Common Toxicity Criteria from the National Cancer Institute. Information on normal tissue toxicity from radionuclides is more limited than that from external beam radiation and is more variable. Variability is likely due to many biologic factors as well as less precise dose quantitation than those used in external beam radiation practice. As expected based on known radiobiologic effects, tolerance to radionuclide therapy appears to exceed that from high dose rate external beam radiation in most organs. Although the correlation between reported dose estimates and toxicity has progressively and substantially improved over the past two decades, further progress is needed to establish optimal toxicity predictive relationships. Continued refinement of dosimetry techniques and standardization is expected to increase the accuracy and comparability of radiation dose reports between institutions as well as improve dose/response correlation.

L77 ANSWER 25 OF 56 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000411359 EMBASE
TITLE: Phase I trial results of iodine-131-labeled antitenascin monoclonal antibody **81C6** treatment of patients with newly diagnosed malignant gliomas.
AUTHOR: Cokgor I.; Akabani G.; Kuan C.-T.; Friedman H.S.; Friedman A.H.; Coleman R.E.; McLendon R.E.; Bigner S.H.; Zhao X.-G.; Garcia-Turner A.M.; Pegram C.N.; Wikstrand C.J.; Shafman T.D.; Herndon II J.E.; Provenzale J.M.; Zalutsky M.R.; Bigner D.D.
CORPORATE SOURCE: Dr. I. Cokgor, Department of Medicine, Duke University Medical Center, Box 3624, Durham, NC 27710, United States. cokgo001@mc.duke.edu
SOURCE: Journal of Clinical Oncology, (15 Nov 2000) 18/22 (3862-3872).
Refs: 29
ISSN: 0732-183X CODEN: JCONDN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 008 Neurology and Neurosurgery
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Purpose: To determine the maximum-tolerated dose (MTD) of iodine-131 (131I)-labeled 81C6 antitenascin monoclonal antibody (mAb) administered clinically into surgically created resection cavities (SCRCs) in malignant glioma patients and to identify any objective responses with this treatment. Patients and Methods: In this phase I trial, newly diagnosed patients with malignant gliomas with no prior external-beam therapy or chemotherapy were treated with a single injection of 131I-labeled 81C6 through a Rickham reservoir into the resection cavity. The initial dose was 20 mCi and escalation was in 20-mCi increments. Patients were observed for toxicity and response until death or for a minimum of 1 year after treatment. Results: We treated 42 patients with 131I-labeled 81C6 mAb in administered doses up to 180 mCi. Dose-limiting toxicity was observed at doses greater than 120 mCi and consisted of delayed neurotoxicity. None of the patients developed major hematologic toxicity. Median survival for patients with glioblastoma multiforme and for all patients was 69 and 79 weeks, respectively. Conclusion: The MTD for administration of 131I-labeled 81C6 into the SCRC of newly diagnosed patients with no prior radiation therapy or chemotherapy was 120 mCi. Dose-limiting toxicity was delayed neurologic toxicity. We are encouraged by the survival and toxicity and by the low 2.5% prevalence of debulking surgery for symptomatic radiation necrosis. (C) 2000 by American Society of Clinical Oncology.

L77 ANSWER 26 OF 56 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000247772 EMBASE
TITLE: Glioma: Novel considerations and treatment modalities.
AUTHOR: Tomera J.F.
CORPORATE SOURCE: J.F. Tomera, 354 South Street, Medfield, MA 02052-3127, United States
SOURCE: Drugs of Today, (2000) 36/6 (355-367).
Refs: 58
ISSN: 0025-7656 CODEN: MDACAP

COUNTRY: Spain
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Glioma tumors often evade traditional cancer treatments and quickly invade healthy brain tissue. Current clinical perspective focuses on the invasiveness of glioma cells which follow distinct anatomic structures within the central nervous system. Advances in magnetic resonance imaging have made it the procedure of choice for identifying brainstem gliomas and classifying them anatomically. Etiologic considerations include adhesion, migration, invasiveness, cell proliferation, angiogenesis and neurotoxin release. This review examines various novel interventions used in treating these deadly growths to prolong life. Recent interventional studies, detecting the cancer's unique characteristics, include the mechanisms that help it survive and spread throughout the brain. Current therapies include those that target glioma cells only, limit the spread of the cancer or block molecules which sustain the tumor. A variety of specific agents, general chemotherapy, radiotherapy and surgery are discussed. (C) 2000 Prous Science.

L77 ANSWER 27 OF 56 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1998191403 EMBASE
TITLE: Iodine-131-labeled antitenascin monoclonal antibody 81C6 treatment of patients with recurrent malignant gliomas: Phase I trial results.
AUTHOR: Bigner D.D.; Brown M.T.; Friedman A.H.; Coleman R.E.; Akabani G.; Friedman H.S.; Thorstad W.L.; McLendon R.E.; Bigner S.H.; Zhao X.-G.; Pegram C.N.; Wikstrand C.J.; Herndon II J.E.; Vick N.A.; Paleologos N.; Cokgor I.; Provenzale J.M.; Zalutsky M.R.
CORPORATE SOURCE: Dr. D.D. Bigner, Duke University Medical Center, Pathology, Box 3156, Durham, NC 27710, United States. bigne001@mc.duke.edu
SOURCE: Journal of Clinical Oncology, (1998) 16/6 (2202-2212). Refs: 46
ISSN: 0732-183X CODEN: JCONDN
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Purpose: To determine the maximum-tolerated dose (MTD) of iodine 131 (131I)-labeled 81C6 monoclonal antibody (mAb) in brain tumor patients with surgically created resection cavities (SCRCs) and to identify any objective responses to this treatment. Methods: In this phase I trial, eligible patients were treated with a single injection of 131I-labeled 81C6. Cohorts of three to six patients were treated with escalating dosages of 131I (starting dose of 20 mCi with a 20-mCl escalation in subsequent cohorts) administered through an Ommaya reservoir in the SCRC. Patients were followed up for toxicity and response until death or for a minimum of 1 year after treatment. The SCRC patients, who were previously irradiated, were followed up without additional treatment unless progressive disease was identified. Results: We administered 36 treatments of 131I doses up to 120 mCi to 34 previously irradiated patients with

recurrent or metastatic bran tumors. Dose-limiting toxicity was reached at 120 mCi and was limited to neuro-logic or hematologic toxicity. None of the patients treated with less than 120 mCi developed significantly neurologic toxicity; one patient developed major hematologic toxicity (MHT). The estimated median survival for patients with glioblastoma multiforme (GBM) and for all patients was 56 and 60 weeks, respectively. Conclusion: The MTD for administration of 131I- labeled 81C6 into the SCRCs of previously irradiated patients with recurrent primary or metastatic brain tumors was 100 mCi. The dose-limiting toxicity was neurologic toxicity. We are encouraged by the minimal toxicity and survival in this phase I trial. Radiolabeled mAbs may improve the current therapy for brain tumor patients.

L77 ANSWER 28 OF 56 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 96106033 EMBASE
DOCUMENT NUMBER: 1996106033
TITLE: **Radioimmunotherapy**: Recent results and future directions.
AUTHOR: Wilder R.B.; DeNardo G.L.; DeNardo S.J.
CORPORATE SOURCE: Molecular Cancer Institute, 1508 Alhambra Blvd,Sacramento, CA 95816, United States
SOURCE: Journal of Clinical Oncology, (1996) 14/4 (1383-1400). ISSN: 0732-183X CODEN: JCONDN
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
023 Nuclear Medicine
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Purpose: To review antibody structure, function, and production; suitable radioisotopes for radioimmunotherapy; challenges facing the field; recent clinical results; toxicity; and future directions. Design: The radioimmunotherapy literature was reviewed, with an emphasis on clinical results and future directions. Results: The highest complete response rates (overall, 50%) have been achieved in patients with B-cell non-Hodgkin's lymphoma. Challenges that currently face radioimmunotherapy include circulating free antigen, binding of antibodies to nonspecific Fc receptors, insufficient tumor penetration, antigenic heterogeneity and insufficient antigen expression, antigenic modulation, and development of human antimouse antibodies. Possible approaches to these challenges, including high-dose radioimmunotherapy and chemotherapy followed by autologous bone marrow transplantation, the use of radionuclides such as yttrium 90 (90Y) and copper 67 (67Cu), and the development of humanized and bifunctional antibodies, are under investigation. Conclusion: Although radioimmunotherapy is a relative new field, substantial progress has been made. Additional research will ultimately resolve many of the challenges that currently face radioimmunotherapy and hopefully lead to the cure of some currently incurable malignancies.

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ACCESSION NUMBER: 96201588 EMBASE
DOCUMENT NUMBER: 1996201588
TITLE: Intrathecal 131I-labeled antitenascin monoclonal antibody 81C6 treatment of patients with leptomeningeal neoplasms or primary brain tumor resection cavities with subarachnoid

communication: Phase I trial results.
AUTHOR: Brown M.T.; Coleman R.E.; Friedman A.H.; Friedman H.S.; McLendon R.E.; Reiman R.; Felsberg G.J.; Tien R.D.; Bigner S.H.; Zalutsky M.R.; Zhao X.G.; Wikstrand C.J.; Pegram C.N.; Herndon II J.E.; Vick N.A.; Paleologos N.; Fredericks R.K.; Schold Jr. S.C.; Bigner D.D.
CORPORATE SOURCE: Duke University Medical Center, P. O. Box 3963,Durham, NC 27710, United States
SOURCE: Clinical Cancer Research, (1996) 2/6 (963-972).
ISSN: 1078-0432 CODEN: CCREF4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
008 Neurology and Neurosurgery
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We aimed to determine the maximum tolerated dose (MTD) of 131I-labeled 81C6 in patients with leptomeningeal neoplasms or brain tumor resection cavities with subarachnoid communication and to identify any objective responses. 81C6 is a murine IgG monoclonal antibody that reacts with tenascin in gliomas/carcinomas but does not react with normal adult brain. 131I- labeled 81C6 delivers intrathecal (IT) radiation to these neoplasms. This study was a Phase I trial in which patients were treated with a single IT dose of 131I-labeled 81C6. Cohorts of three to six patients were treated with escalating doses of 131I (starting dose, 40 mCi; 20 mCi escalations) on 10 mg 81C6. MTD is defined as the highest dose resulting in serious toxicity in no more than two of six patients. Serious toxicity is defined as grade III/IV nonhematological toxicity or major hematological toxicity. We treated 31 patients (8 pediatric and 23 adult). Eighteen had glioblastoma multiforme. Patients were treated with 131I doses from 40 to 100 mCi. Hematological toxicity was dose limiting and correlated with the administered 131I dose. No grade III/IV nonhematological toxicities were encountered. A partial response occurred in 1 patient and disease stabilization occurred in 13 (42%) of 31 patients. Twelve patients are alive (median follow-up, > 320 days); five are progression free >409 days median posttreatment. The MTD of a single IT administration of 131I-labeled 81C6 in adults is 80 mCi 131I- labeled 81C6. The MTD in pediatric patients was not reached at 131I doses up to 40 mCi normalized for body surface area.

L77 ANSWER 30 OF 56 EMBASE
on STN
ACCESSION NUMBER: 95214071 EMBASE
DOCUMENT NUMBER: 1995214071
TITLE: Phase I studies of treatment of malignant gliomas and neoplastic meningitis with 131I-radiolabeled monoclonal antibodies anti-tenascin 81C6 and anti-chondroitin proteoglycan sulfate Mel-14 F(ab')2 - A preliminary report.
AUTHOR: Bigner D.D.; Brown M.; Coleman R.E.; Friedman A.H.; Friedman H.S.; McLendon R.E.; Bigner S.H.; Zhao X.-G.; Wikstrand C.J.; Pegram C.N.; Kerby T.; Zalutsky M.R.
CORPORATE SOURCE: Department of Pathology, Duke University Medical Center, Box 3156,Durham, NC 27710, United States
SOURCE: Journal of Neuro-Oncology, (1995) 24/1 (109-122).
ISSN: 0167-594X CODEN: JNODD2
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 008 Neurology and Neurosurgery
016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The advent of monoclonal antibody (MAb) technology has made Ehrlich's postulate of the 'magic bullet' an attainable goal. Although specific localization of polyvalent antibodies to human gliomas was demonstrated in the 1960s, the lack of specific, high affinity antibody populations and of defined target antigens of sufficient density precluded therapeutic applications. Not until the identification of operationally specific tumor- associated antigens (present in tumor tissue but not normal central nervous system tissue); production of homogeneous, high affinity MAbs to such antigens; and the use of compartmental administration (intrathecal or intracystic), has the promise of passive immunotherapy of primary and metastatic central nervous system neoplasms been recognized. We report here preliminary data from Phase I studies of the compartmental administration of the anti-tenascin MAb 81C6 and F(ab2)2 fragments of MAb Mel-14, which recognizes the proteoglycan chondroitin sulfate-associated protein of gliomas and melanomas, to patients with primary central nervous system tumors or tumors metastatic to the central nervous system. Phase I dose escalation studies of intracystically administered 131I-labeled anti-tenascin MAb 81C6 to either spontaneous cysts of recurrent gliomas or surgically created cystic resection cavities have resulted in striking responses. Of five patients with recurrent cystic gliomas treated, four had partial responses, clinically or radiographically. Similarly, in patients with surgically created resection cavities, a partial response at the treatment site and extended stable disease status has been obtained following intracystic administration of 131I-labeled 81C6. No evidence of hematologic or neurologic toxicity has been observed in either patient population, with the exception of transient exacerbation of a pre-existing seizure disorder in a single patient. Dosimetry calculations indicated high intracystic retention for four to six weeks with little or no systemic dissemination; estimated total doses intracystically ranged from 12,700-70,290 rad. Intrathecal administration of labeled MAbs to patients with neoplastic meningitis is more difficult to assess in terms of clinical responsiveness. Of patients so treated with either 131I-labeled 81C6 or 131I-labeled Mel-14 F(ab)2, cerebrospinal fluid and radiographic responses have been achieved, and survival prolongation through maintenance of stable disease has been observed in several cases. Initial results from Phase I dose escalation trials are encouraging in terms of the proportion of cases of disease stabilization and partial and complete responses obtained. Importantly, neurotoxicity has been virtually nonexistent, and hematologic toxicity rare and rapidly responsive to treatment. In the intracompartmental setting, then, the promise of chimerized MAb molecules or of dimeric or monomeric single-fragment chains, either radiolabeled or drug- or toxin-conjugated, is great. The possibilities of MAb-mediated, targeted therapy for tumors of the central nervous system are many and promising. Future work will be with newly de fined antigens of exquisite tumor specificity, such as the variant epidermal growth factor receptor III molecule. New labeling technology will allow halogens such as 131I and 211At to be used for internalized or membrane-localized antigens. Internalized MAbs will be able to be used as immunotoxins or labeled with chemotherapeutic agents.

L77 ANSWER 31 OF 56 EMBASE
on STN
ACCESSION NUMBER: 94283413 EMBASE

DOCUMENT NUMBER: 1994283413
TITLE: Radioimmunotherapy of neoplastic meningitis in rats using an α-particle- emitting immunoconjugate.
AUTHOR: Zalutsky M.R.; McLendon R.E.; Garg P.K.; Archer G.E.; Schuster J.M.; Bigner D.D.
CORPORATE SOURCE: Department of Radiology, Duke University Medical Center, Box 3808,Durham, NC 27710, United States
SOURCE: Cancer Research, (1994) 54/17 (4719-4725).
ISSN: 0008-5472 CODEN: CNREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
023 Nuclear Medicine
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Because of their short range and high linear energy transfer, α-particles may be particularly effective in the treatment of neoplastic meningitis. Monoclonal antibody 81C6 was labeled with α-particle-emitting 211At using N-succinimidyl3-[211At]astatobenzoate, and the efficacy and toxicity of this immunoconjugate were evaluated in an athymic rat model. Animals were given injections via a chronic indwelling catheter with 5 x 105 TE-671 human rhabdomyosarcoma cells and treated 8 days later with single intrathecal doses of either saline or 4-18 μCi of 211At-labeled specific 81C6 antibody or isotype-matched control 211At-labeled 45.6 antibody. In the first experiment, 4, 7, and 13 μCi 211At-labeled 81C6 produced statistically significant (P = 0.004-0.02) increases in median survival of 33, 29, and 51%, respectively, as compared with saline. Two of 10 animals receiving the 13- μCi dose lived for 6 months before being killed for histological analysis. In the second experiment, 12 μCi of 211At-labeled 45.6 did not increase median survival significantly relative to saline control, while 12 μCi of 211At-labeled 81C6 increased median survival by 113% (P < 0.005) and resulted in 33% apparent cures. Five of 10 animals receiving 18 μCi of 211At-labeled 81C6 survived until they were killed at 295 days. An additional study was performed in animals given intrathecal injections of 5 x 106 TE-671 cells and given a single dose of 18 μCi of 211At-labeled 81C6 or 211At-labeled 45.6. At this higher cell number, significantly prolonged survival was still seen for specific antibody as compared with saline (P < 0.001) and control antibody (P < 0.05). These results suggest that treatment with 211At-labeled monoclonal antibodies may be a valuable approach for neoplastic meningitis.

L77 ANSWER 32 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:376808 BIOSIS
DOCUMENT NUMBER: PREV200300376808
TITLE: Targeted radiotherapy of brain tumours.
AUTHOR(S): Zalutsky, Michael R. [Reprint Author]
CORPORATE SOURCE: Department of Radiology, Duke University Medical Center, Durham, NC, USA
SOURCE: British Journal of Cancer, (July 2003) Vol. 88, No. Supplement 1, pp. S6. print.
Meeting Info.: British Cancer Research Meeting 2003. Bournemouth, UK. July 02-05, 2003.
ISSN: 0007-0920 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English

ENTRY DATE: Entered STN: 13 Aug 2003
Last Updated on STN: 13 Aug 2003

L77 ANSWER 33 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2003:24842 BIOSIS
DOCUMENT NUMBER: PREV200300024842
TITLE: Vascular targeted endoradiotherapy of tumors using alpha-particle-emitting compounds: Theoretical analysis.
AUTHOR(S): Akabani, Gamal [Reprint Author]; McLendon, Roger E.; Bigner, Darrell D.; Zalutsky, Michael R.
CORPORATE SOURCE: Dept. of Radiology, Duke University Medical Center, Box 3808, Durham, NC, 27710, USA
akaba001@mc.duke.edu
SOURCE: International Journal of Radiation Oncology Biology Physics, (November 15 2002) Vol. 54, No. 4, pp. 1259-1275. print.
ISSN: 0360-3016 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Jan 2003
Last Updated on STN: 1 Jan 2003

AB Purpose: To establish the theoretical framework and study the feasibility of 211At-labeled anti-**tenascin** chimeric **81C6** **monoclonal antibody** (mAb) as anti-vascular endoradiotherapy for the treatment of glioblastoma multiforme (GBM) tumors. Methods and Materials: The morphology of blood vessels from histologic images was analyzed and used along with reaction-diffusion equations to assess the activity concentration of 211At-labeled chimeric **81C6** mAb in GBM tumor and normal-brain tissue. Alpha particle microdosimetry was then used to assess the survival probability and average absorbed dose for tumor and normal tissue endothelial cells (ECs) per unit vascular cumulated activity concentration qsource (MBq-s g-1). In turn, these survival probabilities were used to assess the probability of failure PHI for a single vessel. Furthermore, using the vessel density, the specific tumor control probability per unit mass of tumor tissue (tcp) and the specific normal-tissue complication probability per unit mass of normal-brain tissue (ntcp) were estimated. The specific tumor control probability, tcp, was used to assess the overall tumor control probability (TCP) as a function of tumor mass. Results: The levels of 211At-labeled ch81C6 mAb cumulated activity concentration in GBM tumor tissue were approximately five times higher than that in normal-brain tissue. Thus, the average absorbed dose to tumor ECs was higher than that of normal tissue ECs, and the survival probability for GBM ECs was lower than for normal-brain tissue ECs. Consequently, the resulting vessel-failure probability, PHI, for GBM tumor and for normal-brain tissue differ considerably, yielding a qsource range between 103 and 104 MBq-s g-1. Conclusions: This theoretical analysis demonstrated that 211At-labeled chimeric **81C6** is an effective antivascular therapy for the treatment of GBM tumors, yielding a tcp higher than 0.999 for vascular cumulated activity concentrations qsource higher than 1X104 MBq-s g-1, while yielding a low probability for normal-brain tissue damage.

L77 ANSWER 34 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:386709 BIOSIS
DOCUMENT NUMBER: PREV200200386709
TITLE: F(ab')2 construct of human/mouse chimeric (ch) **monoclonal** anti-**tenascin antibody** **81C6** evaluated for radioimmunotherapy of malignant gliomas.

AUTHOR(S): Boskovitz, Abraham [Reprint author]; Pegram, Charles [Reprint author]; LeGrand, Holly [Reprint author]; Zalutsky, Michael R. [Reprint author]; Bigner, Darell D. [Reprint author]
CORPORATE SOURCE: Brain Tumor Program - Depts of Pathology and Radiology, Duke University Medical Center, Durham, NC, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2002) Vol. 43, pp. 255. print. Meeting Info.: 93rd Annual Meeting of the American Association for Cancer Research. San Francisco, California, USA. April 06-10, 2002. ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Jul 2002 Last Updated on STN: 17 Jul 2002

L77 ANSWER 35 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:572427 BIOSIS
DOCUMENT NUMBER: PREV200100572427
TITLE: High-level production of alpha-particle-emitting 211At and preparation of 211At-labeled antibodies for clinical use.
AUTHOR(S): Zalutsky, Michael R. [Reprint author]; Zhao, Xiao-Guang; Alston, Kevin L.; Bigner, Darell
CORPORATE SOURCE: Department of Radiology, Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Journal of Nuclear Medicine, (October, 2001) Vol. 42, No. 10, pp. 1508-1515. print. CODEN: JNMEAQ. ISSN: 0161-5505.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Dec 2001 Last Updated on STN: 25 Feb 2002

AB In vitro and in vivo studies in human glioma models suggest that the antitenascin **monoclonal antibody 81C6** labeled with the 7.2-h-half-life alpha-particle emitter 211At might be a valuable endoradiotherapeutic agent for the treatment of brain tumors. The purpose of this study was to develop methods for the production of high levels of 211At and the radiosynthesis of clinically useful amounts of 211At-labeled human/mouse chimeric **81C6** antibody. Methods: 211At was produced through the 209Bi(alpha, 2n)211At reaction using an internal target system and purified by a dry distillation process. Antibody labeling was accomplished by first synthesizing N-succinimidyl 3-(211At)astatobenzoate from the corresponding tri-n-butyl tin precursor and reacting it with the antibody in pH 8.5 borate buffer. Quality control procedures consisted of methanol precipitation, size-exclusion high-performance liquid chromatography (HPLC), and pyrogen and sterility assays, as well as determination of the immunoreactive fraction by a rapid procedure using a recombinant **tenascin** fragment coupled to magnetic beads. Results: A total of 16 antibody labeling runs were performed. Using beam currents of 50-60 muA alpha-particles and irradiation times of 1.5-4.5 h, the mean 211At production yield was 27.75+-2.59 MBq/muAcntdoth, and the maximum level of 211At produced was 6.59 GBq after a 4-h irradiation at 55 muA. The decay-corrected distillation yield was 67%+-16%. The yield for the coupling of the 211At-labeled active ester to the antibody was 76%+-8%. The fraction of 211At activity that eluted with a retention time corresponding to intact IgG on HPLC was 96.0%+-2.5%. All preparations had a pyrogen level of <0.125 EU/mL and were determined to be sterile. The mean immunoreactive

fraction for these 16 preparations was 83.3%+-5.3%. Radiolysis did not interfere with labeling chemistry or the quality of the labeled antibody product. Conclusion: These results show that it is feasible to produce clinically relevant activities of 211At-labeled antibodies and have permitted the initiation of a phase I trial of 211At-labeled chimeric **81C6** administered directly into the tumor resection cavities of brain tumor patients.

L77 ANSWER 36 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:507580 BIOSIS
DOCUMENT NUMBER: PREV200100507580
TITLE: Results of a Phase II trial in the treatment of newly diagnosed patients with high grade glioma treated with Iodine 131 murine anti-**tenascin** **monoclonal antibody 81C6** via surgically created resection cavities.
AUTHOR(S): Reardon, David A. [Reprint author]; Akabani, Gamal; Friedman, Allan H.; Friedman, Henry S.; Herndon, James E.; Cokgor, Ilkcan; McLendon, Roger E.; Quinn, Jennifer A.; Rich, Jeremy N.; Regalado, Lorna V.; Sampson, John H.; Shafman, Timothy D.; Wong, Terence Z.; Zalutsky, Michael R.; Bigner, Darell D.
CORPORATE SOURCE: Duke University Medical Center, Durham, NC, USA
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 700. print. Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research. New Orleans, LA, USA. March 24-28, 2001. ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 31 Oct 2001 Last Updated on STN: 23 Feb 2002

L77 ANSWER 37 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:141490 BIOSIS
DOCUMENT NUMBER: PREV200000141490
TITLE: Dosimetry and dose-response relationships in newly diagnosed patients with malignant gliomas treated with iodine-131-labeled anti-**tenascin** **monoclonal antibody 81C6** therapy.
AUTHOR(S): Akabani, Gamal [Reprint author]; Cokgor, Ilkcan; Coleman, R. Edward; Gonzalez Trotter, Dinko; Wong, Terence Z.; Friedman, Henry S.; Friedman, Allan H.; Garcia-Turner, Ana; Herndon, James E., II; DeLong, David; McLendon, Roger E.; Zhao, Xiao-Guang; Pegram, Charles N.; Provenzale, James M.; Bigner, Darell D.; Zalutsky, Michael R.
CORPORATE SOURCE: Department of Radiology, DUMC 3808, Durham, NC, 27710, USA
SOURCE: International Journal of Radiation Oncology Biology Physics, (March, 2000) Vol. 46, No. 4, pp. 947-958. print. CODEN: IOBPD3. ISSN: 0360-3016.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Apr 2000 Last Updated on STN: 4 Jan 2002
AB Purpose: The objective of this study was to perform the dosimetry and evaluate the dose-response relationships in newly diagnosed patients with malignant brain tumors treated by direct injections of 131I-labeled

81C6 monoclonal antibody (MAb) into surgically created resection cavities (SCRCs). Methods and Materials: Absorbed doses to the 2-cm-thick shell as measured from the margins of the resection cavity interface were estimated for 42 patients with primary brain tumors. MR images were used to assess the enhanced-rim volume as a function of time after radiolabeled MAb therapy. Biopsy samples were obtained from 15 patients and 1 autopsy. Results: The average absorbed dose (range) to the 2-cm shell region was 32 (3-59) Gy. For the endpoint of minimal time to MR contrast enhancement, the optimal absorbed dose and initial dose-rate were 43 +- 16 Gy and 0.41 +- 0.10 Gy/h, respectively. There was a correlation between the absorbed dose and dose rate to the shell region and biopsy outcome (tumor recurrence, radionecrosis, and tumor recurrence and/or radionecrosis). In this Phase I study, the maximum tolerated dose (MTD) was 120 mCi. At this MTD, the estimated average absorbed dose and initial dose rate to the 2-cm shell were 41 (9-89) Gy and 0.51 (0.24-1.13) Gy/h, respectively. These values are in agreement with the optimal values based on the time to MR lesion rim enhancement. Conclusions: The average absorbed dose to the 2-cm shell region varied considerably and mainly depended on cavity volume. In future clinical trials, the administered activity of 131I-labeled **81C6** MAb may be adjusted based on cavity volume in order to deliver the optimal absorbed dose of 43 Gy rather than giving a fixed administered activity.

L77 ANSWER 38 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:236111 BIOSIS
DOCUMENT NUMBER: PREV200000236111
TITLE: The treatment of recurrent patients with brain tumors treated with iodine 131 anti-**tenascin monoclonal antibody 81C6** via surgically created resection cavities: The results of a phase II trial.
AUTHOR(S): Cokgor, I. [Reprint author]; Akabani, G. [Reprint author]; Friedman, A. [Reprint author]; Coleman, R. [Reprint author]; Zalutsky, M. [Reprint author]; McLendon, R. [Reprint author]; Bigner, S. [Reprint author]; Xiao-Guang, Z. [Reprint author]; Pegram, C. [Reprint author]; Wikstrand, C. [Reprint author]; Herndon, J., III [Reprint author]; Provenzale, J. [Reprint author]; Friedman, H. [Reprint author]; Bigner, D. [Reprint author]
CORPORATE SOURCE: Durham, NC, USA
SOURCE: Neurology, (April 11, 2000) Vol. 54, No. 7 Supp. 3, pp. A33. print.
Meeting Info.: 52nd Annual Meeting of the American Academy of Neurology. San Diego, CA, USA. April 29-May 06, 2000. American Academy of Neurology.
CODEN: NEURAI. ISSN: 0028-3878.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Jun 2000
Last Updated on STN: 5 Jan 2002

L77 ANSWER 39 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:536336 BIOSIS
DOCUMENT NUMBER: PREV199900536336
TITLE: Preparation and characterization of anti-**tenascin monoclonal antibody**-streptavidin conjugates for pretargeting applications.
AUTHOR(S): Foulon, Catherine F. [Reprint author]; Bigner, Darell D.;

Zalutsky, Michael R.
CORPORATE SOURCE: Departments of Radiology and Pathology, Duke University Medical Center, DUMC 3808, Durham, NC, 27710, USA
SOURCE: Bioconjugate Chemistry, (Sept.-Oct., 1999) Vol. 10, No. 5, pp. 867-876. print.
CODEN: BCCHES. ISSN: 1043-1802.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1999
Last Updated on STN: 10 Dec 1999

AB Radioimmunopretargeting is based on the separate injection of a modified mAb and the radionuclide and most frequently exploits the very high avidity of biotin for streptavidin (SA). Currently, we are evaluating the therapeutic potential of directly labeled **monoclonal antibody** (mAb) **81C6**, reactive with the extracellular matrix protein **tenascin**, in surgically created glioma resection cavity patients. To be able to investigate pretargeting in this setting, the synthesis of **81C6** mAb-SA conjugates was required. In the current study, we have evaluated five methods for preparing both murine **81C6** (m81C6) and human/mouse chimeric **81C6** (c81C6) SA conjugates with regard to yield, biotin-binding capacity, immunoreactivity, and molecular weight. The **81C6** mAb and SA were coupled by covalent interaction between sulfhydryl groups generated on the mAb via N-succinimidyl-S-acetylthioacetate, dithiothreitol or 2-iminothiolane (2IT), and maleimido-derivatized SA, prepared via sulfosuccinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate (SMCC) or N-succinimidyl-3-(2-pyridyldithio)-propionate. A noncovalent approach involving reaction of a biotinylated mAb, prepared using biotin caproate, and SA also was studied. The evaluation criteria were yield of mAb-SA 215 kDa monomer, as well as conjugate biotin-binding capacity and immunoreactive fraction. The optimal procedure involved activation of m81C6 or c81C6 with 30 equiv of 2IT and reaction of SA with 10 equiv of SMCC and yielded a conjugate with excellent biotin-binding capacity and immunoreactivity. The (125I-labeled m81C6)-2IT-SMCC-SA was stable and did not lose biotin-binding capacity after a 72 h incubation in human glioma cyst fluid in vitro. Although the conjugate was stable in murine serum in vivo, its biotin-binding capacity declined rapidly, consistent with high endogenous biotin levels in the mouse. After injection of the radioiodinated conjugate into athymic mice with subcutaneous D-54 MG human glioma xenografts, high tumor uptake (36.0 +- 10.7% ID/g at 3 days) and excellent tumor:normal tissue ratios were observed.

L77 ANSWER 40 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:270345 BIOSIS
DOCUMENT NUMBER: PREV199900270345
TITLE: Phase I trial of newly diagnosed brain tumor patients treated with 131I-anti-**tenascin** Mab **81C6** via surgically created resection cavities.
AUTHOR(S): Cokgor, Ilkcan [Reprint author]; Akabani, Gamal [Reprint author]; Friedman, Allan [Reprint author]; Coleman, R. E. [Reprint author]; Zalutsky, Michael [Reprint author]; McLendon, Roger E. [Reprint author]; Bigner, Sandra [Reprint author]; Xiao-Guang, Z. [Reprint author]; Pegram, Charles [Reprint author]; Wikstrand, Carol [Reprint author]; Herndon, James [Reprint author]; Provenzale, Jim [Reprint author]; Friedman, Henry S. [Reprint author]; Bigner, Darell D. [Reprint author]
CORPORATE SOURCE: Durham, NC, USA
SOURCE: Neurology, (April 12, 1999) Vol. 52, No. 6 SUPPL. 2, pp. A245. print.

Meeting Info.: 51st Annual Meeting of the American Academy of Neurology. Toronto, Ontario, Canada. April 17-24, 1999. American Academy of Neurology.
CODEN: NEURAI. ISSN: 0028-3878.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Jul 1999
Last Updated on STN: 15 Jul 1999

L77 ANSWER 41 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:187290 BIOSIS
DOCUMENT NUMBER: PREV199800187290
TITLE: Cytotoxicity of alpha-particle-emitting astatine-211-labelled antibody in tumour spheroids: No effect of hyperthermia.
AUTHOR(S): Hauck, M. L.; Larsen, R. H.; Welsh, P. C.; Zalutsky, M. R. [Reprint author]
CORPORATE SOURCE: Dep. Radiol., Duke Univ. Med. Cent., Durham, NC 27710, USA
SOURCE: British Journal of Cancer, (March, 1998) Vol. 77, No. 5, pp. 753-759. print.
CODEN: BJCAAI. ISSN: 0007-0920.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Apr 1998
Last Updated on STN: 12 Aug 1998

AB The high linear energy transfer, alpha-particle-emitting radionuclide astatine-211 (211At) is of interest for certain therapeutic applications; however, because of the 55- to 70-mum path length of its alpha-particles, achieving homogeneous tracer distribution is critical. Hyperthermia may enhance the therapeutic efficacy of alpha-particle endoradiotherapy if it can improve tracer distribution. In this study, we have investigated whether hyperthermia increased the cytotoxicity of an 211At-labelled **monoclonal antibody** (MAb) in tumour spheroids with a radius (approximately 100 mum) greater than the range of 211At a-particles. Hyperthermia for 1 h at 42degree C was used because this treatment itself resulted in no regrowth delay. Radiolabelled chimeric MAb **81C6** reactive with the extracellular matrix antigen **tenascin** was added to spheroids grown from the D-247 MG human glioma cell line at activity concentrations ranging from 0.125 to 250 kBq ml-1. A significant regrowth delay was observed at 125 and 250 kBq ml-1 in both hyperthermia-treated and untreated spheroids. For groups receiving hyperthermia, no increase in cytotoxicity was seen compared with normothermic controls at any activity concentration. These results and those from autoradiographs indicate that hyperthermia at 42degree C for 1 h had no significant effect on the uptake or distribution of this antitenascin MAb in D-247 MG spheroids.

L77 ANSWER 42 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:290878 BIOSIS
DOCUMENT NUMBER: PREV199800290878
TITLE: Results of a Phase I trial of patients with recurrent brain tumors and prior radiation therapy treated with 131I-labeled anti-**tenascin monoclonal antibody 81C6** via surgically created resection cavities.
AUTHOR(S): Cokgor, Ilkcan; Akabani, Gamal; Brown, Mark T.; Friedman, Alan H.; Coleman, R. Edward; Friedman, Henry S.; Thorstad, Wade L.; McLendon, Roger E.; Bigner, Sandra H.; Zhao, Xiao-Guang; Pegram, Charles N.; Wikstrand, Carol J.;

Herndon, James E.; Vick, Nicholas A.; Paleolog, Nina; Zalutsky, Michael R.; Bigner, D.
CORPORATE SOURCE: Durham, NC, USA
SOURCE: Neurology, (April, 1998) Vol. 50, No. 4 SUPPL. 4, pp. A354. print.
Meeting Info.: 50th Annual Meeting of the American Academy of Neurology. Minneapolis, Minnesota, USA. April 25-May 2, 1998. American Academy of Neurology.
CODEN: NEURAI. ISSN: 0028-3878.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Jul 1998
Last Updated on STN: 8 Jul 1998

L77 ANSWER 43 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:128017 BIOSIS
DOCUMENT NUMBER: PREV199800128017
TITLE: The cytotoxicity and microdosimetry of astatine-211-labeled chimeric **monoclonal antibodies** in human glioma and melanoma cells in vitro.
AUTHOR(S): Larsen, Roy H.; Akabani, Gamal; Welsh, Phil; Zalutsky, Michael R. [Reprint author]
CORPORATE SOURCE: Dep. Radiol., Duke Univ. Med. Center, Durham, NC 27710, USA
SOURCE: Radiation Research, (Feb., 1998) Vol. 149, No. 2, pp. 155-162. print.
CODEN: RAREAE. ISSN: 0033-7587.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Mar 1998
Last Updated on STN: 5 Mar 1998

AB The cytotoxicity of alpha-particle-emitting endoradiotherapeutic compounds is of increasing interest because clinical evaluation of these potential therapeutic agents is commencing. Astatine-211 is a radionuclide with a 7.2-h half-life that emits 5.87 and 7.45 MeV alpha particles. In the present work, we have investigated the in vitro cytotoxicity of 211At-labeled chimeric **monoclonal antibodies** (mAbs) in monolayers of D-247 MG human glioma cells and SK-MEL-28 human melanoma cells. The mAbs studied were **81C6**, reactive with the extracellular matrix antigen **tenascin**, Mel-14, directed against the cell membrane antigen proteoglycan chondroitin sulfate, and a nonspecific control mAb, TPS3.2. Cell uptake increased as a function of activity concentration after a 1-h exposure to the 211At-labeled mAbs. The retention of activity was also measured to calculate cumulative activity associated with the cells and the medium. The clonogenic survival as a function of activity concentration was linear in all cases with no detectable shoulder. Microdosimetric analyses were performed based on measured cell geometry, cumulative activity and Monte Carlo transport of alpha particles. Using 18 kBq/ml activity concentration and 1 h of incubation, a two to five times higher activity bound to the microcolonies was found for the specific mAbs compared to the nonspecific mAb. These calculations indicated that a survival fraction of 0.37 was achieved with 0.24-0.28 Gy for D-247 MG cells and 0.27-0.29 Gy for SK-MEL-28 cells. The microdosimetric cell sensitivity, z0, for D-247 MG cells was significantly lower than for SK-MEL-28 cells (0.08 compared to 0.15 Gy). For both cell lines, reduction in survival to 0.37 required an average of only 1-2 alpha-particle hits to the cell nucleus.

L77 ANSWER 44 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:337201 BIOSIS

DOCUMENT NUMBER: PREV199800337201
TITLE: Human IgG2 constant region enhances the in vivo stability of **monoclonal antibody 81C6** compared to its murine parent.
AUTHOR(S): Reist, C. J.; Bigner, D. D.; Zalutsky, M. R.
CORPORATE SOURCE: Duke Univ. Med. Center, Durham, NC, USA
SOURCE: Journal of Nuclear Medicine, (May, 1998) Vol. 39, No. 5 SUPPL., pp. 77P. print.
Meeting Info.: 45th Annual Meeting of the Society of Nuclear Medicine. Toronto, Ontario, Canada. June 7-11, 1998. Society of Nuclear Medicine.
CODEN: JNMEAQ. ISSN: 0161-5505.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Aug 1998
Last Updated on STN: 12 Aug 1998

L77 ANSWER 45 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1996:348616 BIOSIS
DOCUMENT NUMBER: PREV199699070972
TITLE: Phase I studies of radiolabeled 131I-**81C6** anti-**tenascin monoclonal antibody** in patients with recurrent cystic gliomas or surgically created brain tumor resection cavities: Preliminary results.
AUTHOR(S): Brown, M. T.; Coleman, R. E.; Friedman, A. F.; Friedman, H. S.; Perry, J. R.; McLendon, R. E.; Bigner, S. H.; Zalutsky, M. R.; Schold., S. C., Jr.; Bigner, D. D.
CORPORATE SOURCE: Durham, NC, USA
SOURCE: Neurology, (1996) Vol. 46, No. 2 SUPPL., pp. A473.
Meeting Info.: 48th Annual Meeting of the American Academy of Neurology. San Francisco, California, USA. March 23-30, 1996.
CODEN: NEURAI. ISSN: 0028-3878.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Aug 1996
Last Updated on STN: 5 Aug 1996

L77 ANSWER 46 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1995:284908 BIOSIS
DOCUMENT NUMBER: PREV199598299208
TITLE: Phase I studies of radiolabeled 131I **81C6** anti-**tenascin monoclonal antibody** in patients with malignant gliomas and leptomeningeal metastases: Preliminary results.
AUTHOR(S): Brown, Mark T.; Coleman, R. E.; Friedman, A. F.; Friedman, H. S.; McLendon, R. E.; Bigner, S. H.; Zalutsky, M. R.; Schold., S. C., Jr.; Bigner, D. D.
CORPORATE SOURCE: Durham, NC, USA
SOURCE: Neurology, (1995) Vol. 45, No. 4 SUPPL. 4, pp. A193-A194.
Meeting Info.: 47th Annual Meeting of the American Academy of Neurology. Seattle, Washington, USA. May 6-13, 1995.
CODEN: NEURAI. ISSN: 0028-3878.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English

ENTRY DATE: Entered STN: 5 Jul 1995
Last Updated on STN: 2 Aug 1995

L77 ANSWER 47 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1993:528607 BIOSIS
DOCUMENT NUMBER: PREV199396142014
TITLE: Radioiodination of a **monoclonal antibody** using N-succinimidyl-5-iodo-3-pyridinecarboxylate.
AUTHOR(S): Garg, Sudha; Garg, Pradeep K.; Zhao, Xiao-Guang; Friedman, Henry S.; Bigner, Darell D.; Zalutsky, Michael R. [Reprint author]
CORPORATE SOURCE: Duke Univ. Med. Cent., Dep. Radiol., Durham, NC 27710, USA
SOURCE: Nuclear Medicine and Biology, (1993) Vol. 20, No. 7, pp. 835-842.
ISSN: 0969-8051.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Nov 1993
Last Updated on STN: 19 Nov 1993

AB The potential utility of N-succinimidyl 5-iodo-3-pyridinecarboxylate (SIPC) for the radioiodination of **monoclonal antibodies** was investigated. Paired-label studies were performed using the anti-**tenascin** antibody **81C6** in athymic mice bearing subcutaneous D-54 MG human glioma xenografts. Radiolabeling was also done using N-succinimidyl 3-iodobenzoate (SIB). Radioiodination of SIPC and SIB both proceeded in 60-80% yield, but protein coupling efficiencies with SIB were higher (76 +- 16 vs 60 +- 7%). Immunoreactivity and affinity of both preparations were similar. Using SIPC, thyroid uptake was quite low, decreasing from 0.3% at day 1 to 0.05% at day 8. Tumor uptake reached 46 +- 11% injected dose/g at day 1 but declined gradually thereafter. This apparent decline reflected the rapid growth of these xenografts since tumor accumulation expressed as percentage of injected dose remained nearly constant up to day 9. These results suggest that SIPC, like SIB, offers significant advantages for labeling antibodies when compared with conventional protein iodination methods.

L77 ANSWER 48 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1993:344907 BIOSIS
DOCUMENT NUMBER: PREV199396041907
TITLE: Distribution and dosimetry of iodine-123-labeled **monoclonal antibody 81C6** in patients with anaplastic glioma.
AUTHOR(S): Schold, S. Clifford, Jr.; Zalutsky, Michael R. [Reprint author]; Coleman, R. Edward; Glantz, Michael J.; Friedman, Allan H.; Jaszczak, Ronald J.; Bigner, Sandra H.; Bigner, Darell D.
CORPORATE SOURCE: Duke Univ. Med. Cent., Box 3808, Dep. Radiol., Durham, NC 27710, USA
SOURCE: Investigative Radiology, (1993) Vol. 28, No. 6, pp. 488-496.
CODEN: INVRAV. ISSN: 0020-9996.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jul 1993
Last Updated on STN: 3 Jan 1995

AB Rationale and Objectives: **Monoclonal antibody 81C6** reacts with the extracellular matrix antigen, **tenascin**, present on gliomas and other tumors, as well as several normal tissues, including spleen and liver tissue. Single photon emission computed tomography (SPECT) and I-123-labeled **81C6** at various

protein doses were used t maximize tumor to normal tissue uptake ratios. Methods: The distribution of I-123-labeled **monoclonal antibody 81C6** was determined in 16 patients with recurrent gliomas, using SPECT. Between 3.5 and 11.5 mCi of I-123 were administered to each patient, and the antibody doses were between 10.0 and 100.0 mg. Blood was obtained for pharmacokinetic studies, and patients were imaged 1 hour and 18 hours after antibody administration. Results: All tumors were visualized readily on the SPECT study in areas that corresponded to the contrast, enhancing abnormalities on anatomic neuroimaging studies. The half-life in blood of the I-123 **81C6** ranged from 16 to 37 hours. Radiation dosimetry calculations suggest that it might be possible to administer more than 700 cGy to intracranial glioma with I-131 labeled **81C6** under optimal conditions with acceptable non-neurologic organ radiation exposure. Conclusions: SPECT imaging with I-123 **81C6** identified all tumors and suggests that, with this antibody, more favorable tumor-to-liver and tumor-to-spleen radiation dose ratios are obtained at higher protein doses.

L77 ANSWER 49 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1992:45996 BIOSIS
DOCUMENT NUMBER: PREV199293025971; BA93:25971
TITLE: FOCAL ADHESION INTEGRITY IS DOWNREGULATED BY THE ALTERNATIVELY SPICED DOMAIN OF HUMAN **TENASCIN**.
AUTHOR(S): MURPHY-ULLRICH J E [Reprint author]; LIGHTNER V A; AUKHIL I; YAN Y Z; ERICKSON H P; HOOK M
CORPORATE SOURCE: DEP BIOCHEMISTRY, UNIV ALA BIRMINGHAM, BIRMINGHAM, ALA 35294, USA
SOURCE: Journal of Cell Biology, (1991) Vol. 115, No. 4, pp. 1127-1136.
CODEN: JCLBA3. ISSN: 0021-9525.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 13 Jan 1992
Last Updated on STN: 13 Jan 1992

AB **Tenascin**, together with thrombospondin and SPARC, form a family of matrix proteins that, when added to bovine aortic endothelial cells, caused a dose-dependent reduction in the number of focal adhesion-positive cells to .apprx. 50% of albumin-treated controls. For **tenascin**, a maximum response was obtained with 20-60 μg/ml of protein. The reduction in focal adhesions in **tenascin**-treated spread cells was observed 10 min after addition of the adhesion modulator, reached the maximum by 45 min, and persisted for at least 4 h in the continued presence of **tenascin**. This effect was fully reversible, was independent of de novo protein synthesis, and was neutralized by a polyclonal antibody to **tenascin**. **Monoclonal antibodies** to specific domains of **tenascin** (mAbs **81C6** and 127) were used to localize the active site to the alternatively spliced segment of **tenascin**. Furthermore, a recombinant protein corresponding to the alternatively spliced segment (fibronectin type III domains 6-12) was expressed in Escherichia coli and was active in causing loss of focal adhesions, whereas a recombinant form of a domain (domain 3) containing the RGD sequence had no activity. Chondroitin-6-sulfate effectively neutralized **tenascin** activity, whereas dermatan sulfate and chondroitin-4-sulfate were less active and heparan sulfate and heparin were essentially inactive. Studies suggest that galactosaminoglycans neutralize **tenascin** activity through interactions with cell surface molecules. Overall, our results demonstrate that **tenascin**, thrombospondin, and SPARC, acting as soluble ligands, are able to provoke the loss of focal adhesions in

well-spread endothelial cells.

L77 ANSWER 50 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1990:378669 BIOSIS
DOCUMENT NUMBER: PREV199090065350; BA90:65350
TITLE: **MONOCLONAL ANTIBODY** AND FAB'-2 FRAGMENT DELIVERY TO TUMOR IN PATIENTS WITH GLIOMA COMPARISON OF INTRACAROTID AND INTRAVENOUS ADMINISTRATION.
AUTHOR(S): ZALUTSKY M R [Reprint author]; MOSELEY R P; BENJAMIN J C; COLAPINTO E V; FULLER G N; COAKHAM H P; BIGNER D D
CORPORATE SOURCE: DEP RADIOLOGY, DUKE UNIVERSITY MEDICAL CENTER, BOX 3808, DURHAM, NORTH CAROLINA 27710, USA
SOURCE: Cancer Research, (1990) Vol. 50, No. 13, pp. 4105-4110. CODEN: CNREA8. ISSN: 0008-5472.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 21 Aug 1990
Last Updated on STN: 22 Aug 1990

AB Non-i.v. delivery of radiolabeled **monoclonal antibodies** (MAbs) has been shown to increase tumor uptake and decrease dose to normal tissues. In this study, we have examined the potential advantage of intracarotid (i.c.) versus i.v. administration for the delivery of an intact MAb and a F(ab')2 fragment to tumor in patients with gliomas. Three patients received 10-50 mg of **81C6** IgG2b, a MAb reactive with the glioma-associated extracellular matrix antigen **tenascin**, and three received 5-20 mg of the F(ab')2 fragment of Mel-14, which is reactive with gliomas and melanomas. Paired-injection protocols, in which one-half of the MAb was labeled with 131I and administered by i.c. injection, and one-half was labeled with 125I and simultaneously administered by i.v. injection, were used. For both **81C6** IgG2b and Mel-14 (Fab')2, no differences in blood clearance half-times or urinary excretion rates of radioiodine were observed between i.c.- and i.v.-administered activity. Analysis of biopsy samples revealed i.c.:i.v. uptake lesions of 1.02 ± 0.04, 0.95 ± 0.03, and 1.03 ± 0.05 for the accumulation of **81C6** IgG2b in temporalis muscle, normal brain, and glioma, respectively. Similarly, the i.c.:i.v. uptake ratios for Mel-14 F(ab')2 in these tissues were 0.98 ± 0.04 (SD), 1.00 ± 0.05, and 1.04 ± 0.05. When the differences in percentage of injected dose/g uptake after i.c. and i.v. administration were compared, no statistically significant advantage for i.c. delivery was seen (P = 0.22-0.61). These data indicate that i.c. administration of MAb **81C6** IgG2b and Mel-14 F(ab')2 fragments offers no delivery advantage to offset the small but finite risk involved in cannulation and injection of the internal carotid artery.

L77 ANSWER 51 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1989:516797 BIOSIS
DOCUMENT NUMBER: PREV198988132940; BA88:132940
TITLE: ENHANCED TUMOR LOCALIZATION AND IN-VIVO STABILITY OF A **MONOCLONAL ANTIBODY** RADIOIODINATED USING N SUCCINIMIDYL-3-TRI-N-BUTYLSTANNYLBENZOATE.
AUTHOR(S): ZALUTSKY M R [Reprint author]; NOSKA M A; COLAPINTO E V; GARG P K; BIGNER D D
CORPORATE SOURCE: DEP RADIOL, DUKE UNIV MED CENTER, BOX 3808, DURHAM, NC 27710, USA
SOURCE: Cancer Research, (1989) Vol. 49, No. 20, pp. 5543-5549. CODEN: CNREA8. ISSN: 0008-5472.
DOCUMENT TYPE: Article
FILE SEGMENT: BA

LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 15 Nov 1989
Last Updated on STN: 15 Nov 1989

AB Loss of radiolabel after in vivo administration of labeled **monoclonal antibodies** (MAbs) to cancer patients is a likely cause of the low levels of tumor uptake of MAb which have been observed. In this study, we have evaluated the utility of N-succinimidyl-3-(tri-n-butylstanhyl)benzoate (ATE) for the radioiodination of **81C6**, a MAb reactive with the extracellular matirx antigen **tenascin** associated with gliomas and other tumors. In vitro binding properties of MAb labeled via ATE were slightly better than those of the Iodogen preparations. Paired-label studies were performed in athymic mice bearing s.c. D-54 MG xenografts and injected with both **81C6** labeled with 125I using the ATE method and 131I using the Iodogen method. These studies demonstrated that use of the ATE method (a) decreased thyroid uptake by 40- to 100-fold, suggesting a lower rate of dehalogenation compared to MAb labeled using Iodogen: (b) increased tumor uptake by as much as a factor of 4 at Day 1 to more than 12-fold at Day 8; and (c) resulted in superior tumor-to-normal-tissue dose ratios. The specificity of MAb uptake was investigated in a paired-labeled study comparing the distribuion of **81C6** and isotype-matched control 45.6, both labeled using the ATE procedure. Localization indices for tumor ranged between 6 at Day 1 to 34 at Day 7, values considerably higher than those reported previously for **81C6** and 45.6 radioiodinated using a conventional method (chloramine T). These results demonstrate that the ATE method may be a valuable approach for labeling MAbs with iodine nuclides.

L77 ANSWER 52 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1989:292283 BIOSIS
DOCUMENT NUMBER: PREV198988017627; BA88:17627
TITLE: PHARMACOKINETICS AND TUMOR LOCALIZATION OF IODINE-131-LABELED ANTI-**TENASCIN** **MONOCLONAL ANTIBODY 81C6** IN PATIENTS WITH GLIOMAS AND OTHER INTRACRANIAL MALIGNANCIES.
AUTHOR(S): ZALUTSKY M R [Reprint author]; MOSELEY R P; COAKHAM H B; COLEMAN R E; BIGNER D D
CORPORATE SOURCE: DEP RADIOL, DUKE UNIV MED CENT, DURHAM, NC 27710, USA
SOURCE: Cancer Research, (1989) Vol. 49, No. 10, pp. 2807-2813. CODEN: CNREA8. ISSN: 0008-5472.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 20 Jun 1989
Last Updated on STN: 20 Jun 1989

AB We previously have reported that radioiodinated anti-**tenascin** **monoclonal antibody 81C6** exhibits therapeutic potential against both s.c. and intracranial human glioma xenografts in athymic mice and rats. Herein we report the selective tumor localization of 131I-labeled **81C6** in patients with gliomas and other intracranial malignancies. Nine patients were simultaneously administered 5-50 mg of 131I-labled **81C6** and 1-2 mg of 125I-labeled 45.6, an isotype-matched control **monoclonal antibody**. The blood clearance half-time for **81C6**, normalized to that of 45.6 in the same patient, appeared to decrease with **81C6** protein dose. Gamma camera images obtained at 1 to 3 days exhibited increased uptake of 131I in regions corresponding to tumor with varying degrees of contrast to surrounding normal brain. Biopsy specimens of tumor and normal brain were obtained and analyzed histoologically for tumor content. The average uptake of **81C6** in tumor ranges from 0.6 to 4.3

+ 10-3% of the injected dose per gram. In patients receiving 20-50 mg of **81C6**, the average tumor-to-normal-brain ratio was 25:1 with ratios as high as 200:1 seen in some samples. Localization indices were calculated by normalizing the uptake of **81C6** per gram tumor to the uptake of **81C6** per gram blood and dividing by the same ratio for 45.6 control **monoclonal antibody**. Localization indices for muscle and brain were about 1, in contrast to up to five for tumor. These studies demonstrate that the tumor uptake of 131I-labeled **81C6** in patients with gliomas and other intracranial malignancies is due to specific processes.

L77 ANSWER 53 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1988:312015 BIOSIS
DOCUMENT NUMBER: PREV198886029053; BA86:29053
TITLE: TREATMENT OF INTRACRANIAL HUMAN GLIOMA XENOGRAFTS WITH IODINE-131-LABELED ANTITENASCIN **MONOCLONAL ANTIBODY 81C6**.
AUTHOR(S): LEE Y [Reprint author]; BULLARD D E; HUMPHREY P A; COLAPINTO E V; FRIEDMAN H S; ZALUTSKY M R; COLEMAN R E; BIGNER D D
CORPORATE SOURCE: BOX 3156, DUKE UNIV MED CENT, DURHAM, NC 27710, USA
SOURCE: Cancer Research, (1988) Vol. 48, No. 10, pp. 2904-2910. CODEN: CNREA8. ISSN: 0008-5472.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 3 Jul 1988
Last Updated on STN: 3 Jul 1988

AB Lack of tumor specificity renders current modalities for treating malignant glioma ineffective. The administration of 131I-labeled **monoclonal antibody** (Mab) **81C6**, which reacts with the glioma-associated extracellular matrix antigen, **tenascin**, to nude mice carrying s.c. human glioma xenografts has resulted in significant tumor growth delay and tumor regression. In this study, we evaluated the therapeutic efficacy of 131I-labeled **81C6** in athymic rats bearing intracranial human glioma xenografts, a more appropriate model for human gliomas. Mab **81C6**, an IgG2b immunoglobulin, and an isotype-matched control Mab, 45.6, were labeled at 12.5-23.6 mCi/mg with chloramine-T. The Mabs were given i.v. at 1.25 and 2.5 mCi/animal for 131I-labeled **81C6**, and 1.25 mCi for 131I-labeled 45.6 control. Therapeutic response was evaluated by survival prolongation using Wilcoxon rank sum analysis. Three experiments were done. No significant survival prolongation was found in the trial in which the average tumor size at the time of Mab administration was 60 ± 14 mm3, two-thirds the size which causes animal death. In experiment 2, Mab was given at 16 ± 14 mm3 average intracranial tumor volume. Statistically significant ($P \leq 0.005$) survival prolongation was found for animals treated with 2.5 mCi 131I-labeled **81C6**. In that experiment, male animals with intracranial xenografts had significantly shorter survival than females ($P \leq 0.005$). When only female animals were used in the analysis, the 1.25-mCi **81C6** group also was found to have longer survival benefit ($P \leq 0.01$). In the third experiment, only female animals were used and the tumor size at the initiation of treatment was 20 ± 9 mm3. Highly significant survival prolongation again was found in both 1.25 ($P = 0.001$) and 2.5 mCi ($P < 0.001$) 131I-labeled **81C6** groups. The estimated dose to intracranial tumors after 1.25 mCi of 131I-labeled Mab was 1585 rads for **81C6** and 168 rads for 45.6. Dose to other organs from **81C6** and 45.6 was similar, ranging between 31 rads to the brain and 734 rads to the bone marrow. However, normocellularity was observed

in most marrow tissue examined microscopically. Three animals receiving the low dose (1.25 mCi **81C6**) survived for more than 71 days with apparent cures. In conclusion, intracranial human glioma xenografts were treated successfully with 131I-labeled **81C6** but not control Mab.

L77 ANSWER 54 OF 56 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1988:157616 BIOSIS
DOCUMENT NUMBER: PREV198885081269; BA85:81269
TITLE: THERAPEUTIC EFFICACY OF ANTIGLIOMA MESENCHYMAL EXTRACELLULAR MATRIX IODINE-131-RADIOLABELED MURINE **MONOCLONAL ANTIBODY** IN A HUMAN GLIOMA XENOGRAFT MODEL.
AUTHOR(S): LEE Y-S [Reprint author]; BULLARD D E; ZALUTSKY M R; COLEMAN R E; WIKSTRAND C J; FRIEDMAN H S; COLAPINTO E V; BIGNER D D
CORPORATE SOURCE: BOX 3156, DUKE UNIV MED CENT, DURHAM, NC 27710, USA
SOURCE: Cancer Research, (1988) Vol. 48, No. 3, pp. 559-566. CODEN: CNREA8. ISSN: 0008-5472.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 22 Mar 1988
Last Updated on STN: 22 Mar 1988

AB The development of Mabs, particularly those reactive with primary brain tumors but not with normal brain, provides a potential means of delivering therapeutic agents selectively to human malignant gliomas. Mab **81C6**, an IgG2b immunoglobulin, which defines an epitope of the glioma-associated extracellular matrix protein **tenascin**, has been shown to bind to human glioma cell lines, glioma xenografts in nude mice, and primary human gliomas, but not to normal adult or fetal brain. To test the therapeutic potential of this Mab for targeted delivery of isotopes, nude mice bearing progressively growing s.c. xenografts of D-54 MG, a human glioma cell line, were given injections via the tail vein of either buffer, unlabeled **81C6**, 131I-labeled **81C6**, or 131I-labeled 45.6, a nonspecific control Mab of the same isotype. Specific activities of the Mab range from 6.0 to 15.5 mCi/mg with protein doses from 7.6 to 167 μg. The doses given by injection per animal for labeled **81C6** were 50, 250, 500, and 1000 μCi and 500 and 1000 μCi for 45.6. Tumor response was measured by growth delay in reaching 1000 or 5000 mm3 tumor volumes using the Wilcoxon rank sum test, and by comparing the proportion of tumors that had regression in volume after treatment using the Fisher exact test. Statistially significant growth delays at 1000 mm3 were noted in 1 of 3 experiments with 500 μCi **81C6** ($P < 0.001$) and 2 of 3 for 1000 μCi **81C6** ($P = 0.001$ and < 0.001). At 5000 mm3, statistically, significant growth delays were seen with radiolabeled **81C6** in 2 of 2 experiments at 250 μCi ($P = 0.01$ and 0.02), 4 of 4 at 500 μCi ($P = 0.03 - <0.001$), and 2 of 2 at 1000 μCi ($P = \leq 0.001$) and with radiolabeled 45.6 in 1 of 1 at 1000 μCi ($P = 0.01$). The percentage of animals with tumor regression progressively increased with increasing doses of isotope. For radiolabeled 45.6, there were 0 of 10 regressors at 500 and 1 of 10 at 1000 μCi. For radiolabeled **81C6**, there were 0 of 6 regressors at 50 μCi, 1 of 16 (6%) at 250 μCi, 7 of 38 (18%) at 500, and 15 of 28 (54%) at 1000 μCi. Statistically significant tumor regression was seen only at doses of 500 and 1000 μCi of 131I-**81C6**. The initial tumor size for those regressing was significantly smaller than those not regressing ($P = 0.01$ for 500 μCi and 0.0009 for 1000 μCi). The estimated dose to tumor was 9719 cGy for 1000 μCi **81C6** and 2346 cGy for 1000 μCi 45.6. Doses to other organs for **81C6** and 45.6 were equivalent ranging from 135

cGy for brain to 2415 cGy for lung. Whole body dose determined by total body measurement with dose calibrator and direct individual tissue counting with a gamma counter were equivalent. Comparative dosimetry calculations were made based upon data extrapolated from prior trace-labeled localization studies (5 μCi/5 μg/animal). The estimated radiation dose to tumor from these studies in which no therapeutic response was seen underestimated the dose observed in a directly measured therapeutic trial by 35-52%. In this xenograft model, a radiolabeled antiglioma Mab against the extracellular matrix protein **tenascin** demonstrated therapeutic efficacy. The promising results obtained in this animal model suggest a potential value for this form of therapy against human malignant gliomas.

L77 ANSWER 55 OF 56 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-058513 [05] WPIDS
CROSS REFERENCE: 2001-607195 [69]; 2001-616242 [71]; 2003-854127 [79]
DOC. NO. CPI: C2003-015008
TITLE: Novel enzymatic nucleic acid that down-regulates expression of neurite growth inhibitor receptor, prostaglandin D2 receptor, IkappaB kinase or protein kinase PKR genes, for treating cancer and inflammatory disease.
DERWENT CLASS: B04 B05 D16
INVENTOR(S): BLATT, L; CHOWRIRA, B; MCSWIGGEN, J; MCSWIGGEN, J A; FOSNAUGH, K; HAEBERLI, P
PATENT ASSIGNEE(S): (BLAT-I) BLATT L; (CHOW-I) CHOWRIRA B; (MCSW-I) MCSWIGGEN J; (MCSW-I) MCSWIGGEN J A; (FOSN-I) FOSNAUGH K; (RIBO-N) RIBOZYME PHARM INC
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002081628	A2	20021017	(200305)*	EN	317
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					
US 2003113891	A1	20030619	(200341)		
US 2003119017	A1	20030626	(200343)		
US 2003143732	A1	20030731	(200354)		
US 2003148507	A1	20030807	(200358)		
US 2003191077	A1	20031009	(200367)		
EP 1386004	A2	20040204	(200410)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2002081628	A2		WO 2002-US10512	20020403
US 2003113891	A1	Provisional	US 2000-181797P	20000211
		CIP of	US 2001-780533	20010209
			US 2001-827395	20010405
US 2003119017	A1	Provisional	US 2001-294412P	20010529
			US 2002-156306	20020528

US 2003143732	A1	Provisional	US 2001-315315P 20010828
			US 2002-224005 20020820
US 2003148507	A1	Provisional	US 2001-315315P 20010828
			US 2002-226992 20020823
US 2003191077	A1	Provisional	US 2001-315315P 20010828
			US 2002-230006 20020828
EP 1386004	A2		EP 2002-763926 20020403
			WO 2002-US10512 20020403

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 1386004	A2	Based on	WO 2002081628

PRIORITY APPLN. INFO: US 2001-315315P 20010828; US 2001-827395 20010405; US 2001-294412P 20010529; US 2000-181797P 20000211; US 2001-780533 20010209; US 2002-156306 20020528; US 2002-224005 20020820; US 2002-226992 20020823; US 2002-230006 20020828

AB WO 200281628 A UPAB: 20040210

NOVELTY - A nucleic acid molecule (NA) (I), preferably an enzymatic NA selected from NA that down-regulates expression or inhibits function of a receptor for neurite growth inhibitor, NA that down-regulates expression of prostaglandin D2 receptor gene or of NA encoding IkappaB kinase subunit or protein kinase PKR, and NA comprising a sequence (S1) selected from 6182 sequences given in the specification, is new.

DETAILED DESCRIPTION - A nucleic acid molecule (NA) (I), preferably an enzymatic NA selected from NA that down-regulates expression or inhibits function of a receptor for a neurite growth inhibitor, NA that down-regulates expression of a prostaglandin D2 receptor (PTGDR) gene or of NA encoding IkappaB kinase (IKK) subunit or protein kinase PKR, and NA comprising a sequence (S1) selected from 6182 sequences fully defined in the specification, such as a sequence of ggcagcaGgaggaaacucCCUUCaaggacaucg ucCGGGucccaggB.

INDEPENDENT CLAIMS are also included for the following:

(1) an antisense nucleic acid molecule (II) comprising a sequence complementary to a sequence (S2) selected from 4414 sequences fully defined in the specification, such as CAACCCCUACGAUGAAG;

(2) an expression vector (III) comprising (I) in a manner that allows the expression of (I);

(3) a mammalian cell (IV) comprising (I) or (II); and

(4) a pharmaceutical composition (V) comprising (II) or NA selected from NA that down-regulates expression of PTGDR gene or of NA encoding IKK subunit or protein kinase PKR, and NA comprising a sequence selected from 4610 sequences given in the specification.

ACTIVITY - Cytostatic; Antiinflammatory; Antirheumatic; Antiarthritic; Antiasthmatic; Antidiabetic; Immunosuppressive; Vasotropic; Anorectic; Dermatological; Neuroprotective; Nephrotropic; Antibacterial; Antiallergic.

MECHANISM OF ACTION - Down-regulator of NOGO, PKR, IKK, or PTGDR activity in a cell (claimed); Down-regulator of target gene expression; Gene therapy; Antisense therapy. No supporting data is given.

USE - (I) is useful for reducing NOGO receptor activity in a cell, for down-regulating PKR or IKK- gamma activity in a cell, for treating a patient having a condition associated with levels of NOGO receptor, PKR or IKK- gamma , for cleaving RNA encoded by NOGO receptor gene, PKR gene, IKK- gamma gene or PTGDR gene, or for administering (I) to a cell, preferably a mammalian or human cell. (I) or (II) is useful for treating

conditions such as cerebrovascular accident or central nervous system (CNS) injury, where treatment of CNS injury is useful for treating spinal cord injury, for treating cancer (such as breast, lung, prostate, colorectal, brain, esophageal, stomach, bladder, pancreatic, cervical, head, neck, ovarian or multidrug resistant cancer, or melanoma, **lymphoma** or glioma), for treating an inflammatory disease (such as rheumatoid arthritis, restenosis, asthma, Crohn's disease, diabetes, obesity, autoimmune disease, lupus, multiple sclerosis, transplant/graft rejection, gene therapy applications, ischemia/reperfusion injury (CNS and myocardial), glomerulonephritis, sepsis, allergic airway inflammation, inflammatory bowel disease or infection), for reducing PTGDR activity in a cell, for treating a patient having a condition associated with the level of PTGDR, or for treating an allergic condition (such as asthma, allergic rhinitis, or atopic dermatitis). In addition to using (I) or (II), other drug therapies are administered to the patient including **monoclonal antibodies**, IKK-gamma or PKR-specific inhibitors, chemotherapy or radiation therapy. The chemotherapy is paclitaxel, docetaxel, cisplatin, methotrexate, cyclophosphamide, doxorubin, fluorouracil carboplatin, edatrexate, gemcitabine or vinorelbine. (all claimed). (I) is also useful for down-regulating expression of a target gene such as prostaglandin D2 synthetase, adenosine receptors, NI-35, NI-220, NI-250, myelin-associated glycoprotein, **tenascin**-R, or NG-2, or for treating a patient having a condition associated with the level of a target gene. (I) is useful as a diagnostic tool to examine genetic drifts and mutations within diseased cells or to detect the presence of a target RNA in a cell.
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L77 ANSWER 56 OF 56 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-531471 [48] WPIDS
CROSS REFERENCE: 1993-303150 [38]; 1996-097460 [10]; 1997-434333 [40]; 1998-397937 [34]; 1999-105025 [09]; 1999-131255 [11]; 1999-189722 [16]; 1999-579890 [49]; 2000-072047 [06]; 2000-269871 [23]; 2000-363766 [31]; 2001-450473 [48]; 2002-329121 [36]; 2003-182059 [18]; 2004-033626 [03]; 2004-130701 [13]
DOC. NO. CPI: C2000-158393
TITLE: New immunological and growth factor-based bispecific binding ligands, useful for stimulating coagulation in vasculature-associated diseases, e.g. for treating both benign and malignant diseases (e.g. meningioma or hemangioma).
DERWENT CLASS: B04 D16
INVENTOR(S): EDGINGTON, T S; THORPE, P E
PATENT ASSIGNEE(S): (SCRI) SCRIPPS RES INST; (TEXA) UNIV TEXAS SYSTEM
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 6093399	A	20000725	(200048)*		83

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 6093399	A	CIP of	US 1992-846349	19920305
		CIP of	US 1994-205330	19940302
		CIP of	US 1994-273567	19940711
			US 1995-482369	19950607

PRIORITY APPLN. INFO: US 1995-482369 19950607; US 1992-846349 19920305; US 1994-205330 19940302; US 1994-273567 19940711

AB US 6093399 A UPAB: 20040223

NOVELTY - A binding ligand (I) comprising a first binding region that is operatively linked to a coagulation factor, or a second binding region that binds to a coagulation factor, is new.

DETAILED DESCRIPTION - A binding ligand (I) comprising a first binding region that binds to a component expressed, accessible to binding or localized on the surface of a tumor cell, intratumoral vasculature or tumor stroma, is new. The first binding region is operatively linked to a coagulation factor, or a second binding region that binds to a coagulation factor. The second binding region comprises an antibody or an antigen binding region of an antibody.

INDEPENDENT CLAIMS are also included for the following:

(1) a binding ligand comprising a first binding region that binds to a component expressed, accessible to binding or localized on the surface of intratumoral vasculature or stroma, where the first binding region is operatively linked to a coagulant or an antibody, or an antigen binding region that binds to a coagulant;

(2) a binding ligand comprising a first antibody or its antigen binding region, which binds to a component expressed, accessible to binding or localized on the surface of intratumoral vasculature or stroma, where the first antibody or antigen binding region is operatively linked to a coagulant or to a second antibody, or antigen binding region that binds to a coagulant;

(3) binding ligands comprising a first antibody or its antigen binding region, which binds to a marker expressed, accessible to binding or localized on the cell surface of intratumoral blood vessels of a vascularized tumor, where the first antibody or antigen binding region is linked to a coagulant or to a second antibody, or its antigen binding region that binds to a coagulant;

(4) a conjugate comprising a first antibody or its antigen binding portion that binds to a marker expressed or localized on the cell surface of intratumoral blood vessels of a vascularized tumor, where the first antibody or antigen binding portion is linked to a coagulant or a second antibody, or an antigen binding region that binds to a coagulant;

(5) binding ligands comprising a first binding region that binds to a component expressed, accessible to binding or localized on the surface of a tumor cell, established intratumoral vasculature, tumor-associated vasculature or tumor stroma, where the first binding region is operatively linked to a coagulation factor or to an antibody or its antigen binding region that binds to a coagulation factor; and

(6) a pharmaceutical composition comprising (I).

ACTIVITY - Cytostatic; coagulant. A20 cells coated with B21-2/10H10 complex and truncated Tissue Factor (tTF) were capable of inducing fibrin formation, it shortened coagulation time from 140 seconds (the time for mouse plasma in CaCl2 to coagulate in the absence of added antibodies or TF under specific conditions) to 60 seconds. Mouse plasma added to A20 cells to which tTF had been tethered with B21-2/10H10 coagulated rapidly. Fibrin strands were visible 36 seconds after addition of plasma as compared with 164 seconds in plasma added to untreated A20 cells.

MECHANISM OF ACTION - Thrombin stimulator. For establishment of solid tumors, 1.5 multiply 107 C1300 cells were injected subcutaneously into the right anterior flank of BALB/c nu/nu mice. When tumors had grown to 0.8 cm in diameter, mice were randomly assigned to treatment groups each containing 7-8 mice. Mice 0.8 cm diameter tumors administered with the coaguligand, composed of B21-2/10H10 and tTF, showed tumor regression to

approximately half their pre-treatment size. Repeated treatment on the 7th day caused the tumors to regress further, usually completely. In 5/7 animals, complete regressions were obtained. These **anti-tumor** effects were statistically highly significant (P is less than 0.001) when compared with all other groups.

USE - The binding ligand is useful for effectively promoting coagulation in intratumoral blood vessels when administered to a subject having vascularized tumor (claimed). It is useful in achieving specific coagulation , e.g. coagulation in tumor vasculature. Furthermore, the binding ligand is useful for stimulating coagulation in vasculature-associated diseases. Particularly, the binding ligand is useful for treating both benign and malignant diseases that have a vascular component. These diseases include benign growths (e.g. BPH), diabetic retinopathy, arteriovenous malformations, meningioma, hemangioma, neovascular glaucoma, psoriasis, synovitis, endometriosis, hemophylic joints, hypertrophic scars or vascular adhesions. The binding ligands may also be combined with **anti-tumor** therapy (e.g. radiotherapy or chemotherapy).

ADVANTAGE - Immunotoxins have proven effective at treating **lymphomas** and leukemias. However, immunotoxins are ineffective in the treatment of solid tumors. Another problem is that antigen-deficient mutants can escape being killed by the immunotoxin and regrow. The present binding ligands offer several advantages. Firstly, the target cells are directly accessible to intravenously administered ligands, permitting rapid localization of high percentage of the injected dose. Secondly, since each capillary provides oxygen and nutrients for thousands of cells in its surrounding cord of tumor, even limited damage to the tumor vasculature could produce an avalanche of tumor cell death. Finally, the outgrowth of mutant endothelial cells, lacking a target antigen, is unlikely because they are normal cells. Thus, the binding ligands are safer for use in humans than that of targeting a toxin to tumor vasculature.

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